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24.

CONFORMATION AND REACTIVITY IN THE
BICYCLO[3.3.2]DECANE SYSTEM

A Thesis

Presented to the University of Stirling for the
Degree of Ph.D

by

RUSSELL HAFNER

July 1973

I should like to thank Professor W. Forster for his advice and encouragement throughout the past two and a half years; his interest and guidance have been a great help during the conduct of this research.

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and

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I should also like to thank Dr. P. and Dr. J. Murray-Rust for their interest in the conformational aspects of this work, and in particular for carrying out the X-ray crystallographic studies described in this thesis.

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My thanks are also due to Miss L. Edward for her expertise in typing this thesis.

Finally, I am grateful to the Science Research Council for a maintenance award for two and a quarter years.

Chemistry especially has always had
irrestible attractions for me from the
enormous, the illimitable power which the
knowledge of it confers. Chemists - I assert
it emphatically - might sway, if they pleased,
the destinies of humanity.

Count Fosco in "The Woman in White."

by Wilkie Collins

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ABSTRACT

The synthesis of a series of substituted bicyclo(3.3.2)decane derivatives is described. Infra-red spectroscopy shows the presence of bands that can only be ascribed to a 3,7-interaction in a twin-chair conformation for many derivatives, but there is evidence for a conformational equilibrium between twin-chair and boat-chair conformations. In cases where the atoms of the two carbon bridge are constrained by a double bond, or an equivalent grouping, so that they are coplanar with the bridgehead atoms, the preferred conformation is the boat-chair; this has been confirmed by the X-ray structure of 7,8,9,10-tetrahydro-6,10-propano-6H-cyclohepta(b)quinoxaline.

Solvolytic studies on exo-2,3-epoxybicyclo(3.3.2)decane are reported. Hydride shifts are found to be more facile than in the bicyclo(3.3.1)nonane system, and a revised mechanistic scheme for the acid catalysed solvolysis of epoxides is described.

Buffered acetolysis of exo-2-bicyclo(3.3.2)decyl tosylate shows two interesting phenomena. Firstly, there appears to be a significant 1,2-hydride shift to the bridgehead position, and secondly, it is probable that a 2,6-hydride shift is taking place in a twin-twist-boat conformation.

9-Bicyclo(3.3.2)decanone has been found to be a surprisingly unreactive ketone; this lack of reactivity is rationalised in terms of I-strain theory.

Preliminary studies into the autoxidation of bicyclo(3.3.2)decane and the synthesis of bicyclo(3.3.2)deca-2,6-diene are reported, the latter in connection with a study into the Single Inversion Cope Reaction.

INTRODUCTION

Table 1

Ring size	Tosylate Solvolysis (k_{rel}) refs. 4,5	Borohydride Reduction (k'_{rel}) ref. 6	Cyanohydrin Dissociation (K) ref. 7
4	11.26	1.64	-
5	13.59	0.044	0.021
6	1	1	0.001
7	25.32	0.006	0.13
8	190.72	0.0005	0.86
9	172.15	0.0002	1.70
10	376.0	0.00008	-
11	48.95	0.00015	1.12
12	3.25	0.0011	0.31
13	3.50	0.0012	0.26

k_{rel} = rate constant relative to cyclohexyl tosylate.

k'_{rel} = rate constant relative to cyclohexanone.

The chemistry dependence upon the internal strain in of torsional, trans more specifically containing from 7 that this field of to these systems. pounds have a very lead to eliminatio is the experimental a medium ring, suc in an equilibrium conversion in a no with the I-strain ring size should be of a bond, such as involving the make That this is in fe rates of solvolys rates of borohydr⁶ alkanones, and the⁷ cyanohydrins. (S

Introduction

The chemistry of carbocyclic rings exhibits a remarkable dependance upon the size of the ring, considered¹⁻³ to be due to internal strain in such rings. This internal strain is a function of torsional, transannular, and angle strain factors. Turning more specifically to the chemistry of medium rings (i.e. those containing from 7 to 11 carbon atoms), it is at once apparent that this field of chemistry shows several unusual facets peculiar to these systems. For example, it is found that medium ring compounds have a very high solvolytic reactivity, and solvolyses often lead to elimination rather than substitution. Connected with this is the experimental difficulty of converting a trigonal centre in a medium ring, such as a carbonyl group, to a tetrahedral system in an equilibrium reaction, and also the slower rate of such a conversion in a non-equilibrium reaction. This is in accordance with the I-strain theory which predicts that opposite effects of ring size should be observed in reactions involving the breaking of a bond, such as tosylate solvolysis; as compared with reactions involving the making of a bond, such as the reduction of ketones. That this is in fact so may be seen by a comparison of the relative rates of solvolysis for cycloalkyl tosylates^{4,5} with the relative rates of borohydride reduction for the corresponding cycloalkanon⁶es, and the dissociation constants for the cycloalkanon⁷es cyanohydrins. (See table 1)

Cyanohydrin
Dissociation
(K)
ref.7

-
0.021

0.001

0.13

0.86

1.70

-
1.12

0.31

0.26

ate.

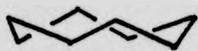
The observed preference for trigonal rather than tetrahedral structures is considered to be due largely to the reduction in transannular strain that results from inclusion of a trigonal carbon atom or atoms in the molecule.

Another characteristic of medium rings is a remarkable tendency to undergo transannular reactions,⁸ which may be either hydride shifts or ring closure reactions. Such reactions are considered to result from the conformational proximity of a C-H bond to a reactive centre across the carbocyclic ring. As an example, one may cite Cope's⁹⁻¹¹ examination of the formolysis of cis-cyclo-octene oxide, where a considerable quantity of cis-cyclo-octane-1,4-diol was formed in addition to the expected trans-cyclo-octane-1,2-diol. Further, several minor products, all formed by transannular pathways, were detected. The factors governing the occurrence of transannular hydride shifts are, in spite of a considerable research effort, particularly by Cope⁸⁻¹² and Prelog,^{13,14} by no means well understood; and Marvell¹⁵ has posed several questions that need to be answered before satisfactory predictions may be made with regard to these processes. Thus, the relative degree of importance of such factors as proximity of a C-H group to the reacting centre, ring strain in the transition state, hindrance to reaction with other molecules and the magnitude of conformational barriers are by no means fully resolved.

Fig 1



crown



stretched crown



boat-chair



saddle



butterfly

A third charac
mobility. To take
the molecule and th
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16
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A third characteristic of medium rings is their conformational mobility. To take as an example cyclo-octane, the flexibility of the molecule and the large number of energetically feasible conformations available to it are at once apparent from a molecular model. It is thus not surprising that there has been considerable argument in the literature concerning its preferred conformation, and crown, stretched crown, boat-chair, saddle, and butterfly conformations have all been proposed at various times (see fig.1). As a result of this conformational mobility, it is difficult to construct theories and make predictions about the reactivity of a given molecule. As a result it has become common practice to study bridged ring systems, in which the conformational flexibility is reduced by bridging the main ring with one or more carbon atoms. In such compounds, the number of factors influencing a given situation are reduced, and so bridged rings are often a fruitful testing ground for theories.

Bicyclo(3.3.2)decane (1) is a fairly typical medium ring, being formally cyclo-octane, constrained by a 1,5 two carbon bridge. At the inception of this work, in September 1970, bicyclo(3.3.2)decane was still a largely unknown system. It first appears in the literature in 1956, in a paper by Alder et. al. who described the deamination of endo-6-aminomethyl-bicyclo(3.2.2)nonane hydrochloride (2) to give exo- and endo-

3-bicyclo(3.3.2)decaneols (3 and 4). When studies of the bicyclo(3.3.2)decane system first began in these laboratories, in 1967, exo-3-bicyclo(3.3.2)decaneol was central to the proposed scheme of ²² research; and so Alder's synthesis was reinvestigated by Doyle. Alder's results were viewed with considerable, and, as it turned out, justified scepticism; particularly since Alder had no access to sophisticated gas chromatographic analytical techniques; since there was no real proof of the bicyclo(3.3.2)decane ring system to the exclusion of others; since, given that the ring system was bicyclo(3.3.2)decane, there was no real proof that the hydroxyl group was at position 3 rather than position 2 in the ring.

On reinvestigation, ²² Alder's synthesis gave not less than ten different compounds, of which the main components were later shown to be exo- and endo-2-bicyclo(3.3.2)decaneols (5 and 6).

There is no further mention until 1963/4, apart from a reference in 1959 to 1,6,6-trimethylbicyclo(3.3.2)dec-9-ene-3-one (7) in a paper describing the construction and use of a nuclear induction ²³ spectrometer, which was used to prove that a certain compound was the above bicyclo(3.3.2)decane derivative rather than an isomer containing a bicyclo(4.2.2)decane skeleton.

In 1963 Schroeder published the first of a series of papers on the chemistry of bullvalene (tricyclo(3.3.2.0^{4,6})deca-2,7,9-triene) (8). Catalytic hydrogenation of bullvalene gives bicyclo(3.3.2)decane itself; and reduction with sodium in liquid ammonia at -78° gives bicyclo(3.3.2)deca-2,6,9-triene (9). Reduction at higher temperatures

gives a mixture of the triene and a $C_{10}H_{14}$ compound that may be bicyclo(3.3.2)deca-2,6-diene (10). Treatment of bullvalene with bromine in methylene chloride, or with sulphuryl chloride yields the appropriate 4,8-dihalogenobicyclo(3.3.2)deca-2,6,9-triene (11). Further bicyclo(3.3.2)decane derivatives have appeared in the literature in the course of studies on bullvalene, particularly a range of transition metal complexes of bicyclo(3.3.2)decane derivatives.

In 1968, Graham published a synthesis and reactivity study of 1,5-bis-methylenecyclo-octane (12), which was reported to ring close to 1-chlorobicyclo(3.3.2)decane (13) and 1-bicyclo(3.3.2)decanol (14) on treatment with a mixture of hydrochloric and acetic acids. The alcohol was independantly synthesised from bicyclo(3.3.2)decan-10-one-1-ol (15), itself the product from an intramolecular aldol condensation of 5-acetylcyclo-octanone (16). However, in 1971 Schleyer synthesised directly from bicyclo(3.3.2)decane itself, the same two bridgehead substituted compounds (13 and 14) that Graham claimed to have prepared. Schleyer's and Graham's data did not agree, and after private correspondence Graham concurred that his alcohol was not 1-bicyclo(3.3.2)decanol. In view of this result, a reexamination of the reactivity of 1,5-bis-methylenecyclo-octane might well be of interest, particularly since a much simpler synthesis of this compound has been developed in these laboratories. These results cast a new light on the results of Graham's

solvolyses of esters of 1-hydroxymethylbicyclo(3.3.1)nonane (17), and of the deamination of 1-aminomethylbicyclo(3.3.1)nonane (18). From these reactions was isolated in all cases varying quantities of a tertiary alcohol, considered to be 1-bicyclo(4.3.1)decanol (19) because of its non-identity with the alcohol at that time believed to be 1-bicyclo(3.3.2)decanol. A material that was gas chromatographically indetical with Graham's spurious 1-bicyclo(3.3.2)decanol²⁸ was isolated only from the deamination reaction, and from buffered acetolysis of 1-tosyloxymethylbicyclo(3.3.1)nonane (20). However, neither buffered acetolysis of the corresponding brosylate, nor solvolysis of the tosylate in any other acid medium gave rise to this tertiary alcohol. The compound assigned as 1-bicyclo(4.3.1)decanol was isolated, and from the data quoted it is different from 1-bicyclo(3.3.2)decanol as prepared by Schleyer. As a result, the question of the true identity of the tertiary alcohol originally assigned as 1-bicyclo(3.3.2)decanol is still unanswered.

Also in 1968; Smith, Kline and French Laboratories took out a patent³³ which included several syntheses of bicyclo(3.3.2)decane derivatives. Bicyclo(3.3.2)decane-1-carboxylic acid (21) was synthesised by a Koch-Haaf reaction on 1-hydroxymethylbicyclo(3.3.1)nonane (17). 2-Acetamidobicyclo(3.3.2)decane (22) was made by a Ritter reaction on 6-hydroxymethylbicyclo(3.2.2)nonane (23). 9-Bicyclo(3.3.2)decanol (24) was prepared by deamination of 9-aminomethylbicyclo(3.3.1)nonane (25). The patent also describes syntheses based on 3-bicyclo(3.3.2)decanol, whose synthesis was not described

but was presumably the alcohol as prepared by Alder.

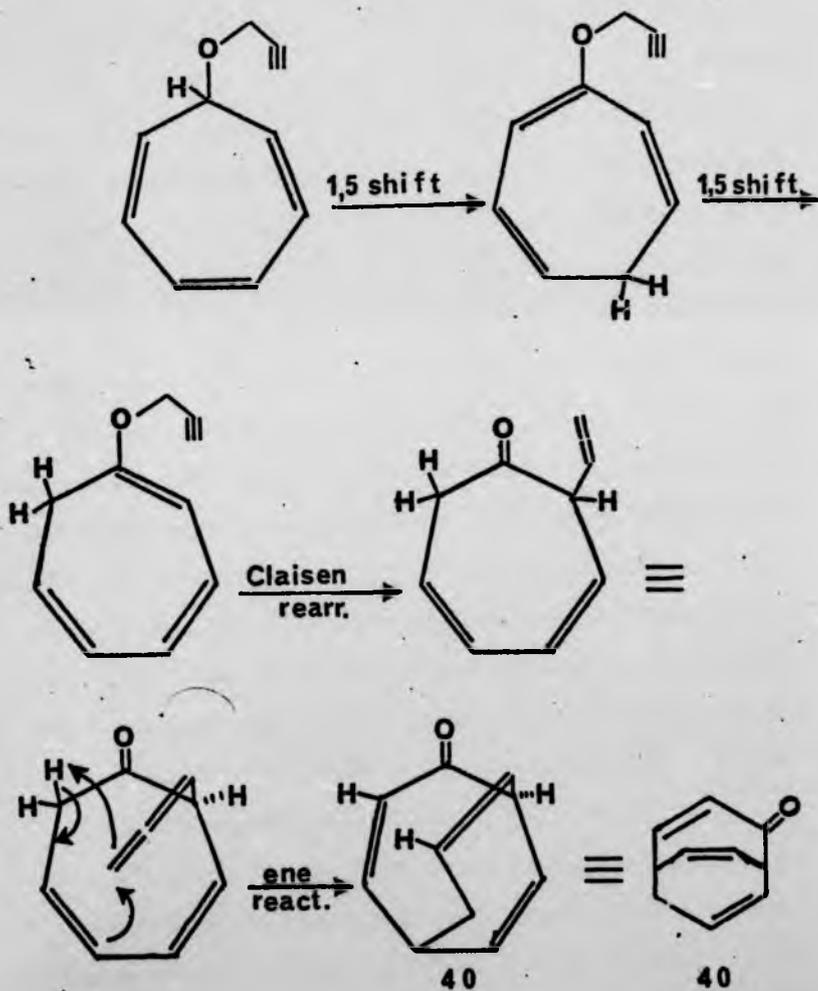
Having found Alder's synthesis to be quite unsuitable for his purpose, Doyle turned ^{34,35} in 1967, to the ring expansion of bicyclo(3.3.1)non-2-ene-9-one (26), a readily available ^{36,37} starting material. Experience with bicyclo(3.3.1)non-2-ene (27) had shown that it was quite practicable to obtain pure exo-2- and exo-3-bicyclo ³⁸ (3.3.1)nonanols (28 and 29) by hydroboration; so it was expected that the desired corresponding alcohols in the bicyclo(3.3.2)decane system should be equally readily available from 2-bicyclo(3.3.2)decene (30); itself available from the ring expansion product of bicyclo(3.3.1)non-2-ene-9-one, namely bicyclo(3.3.2)dec-2(3)-ene-9-one (31 and 32).

Doyle was unable to effect ring expansion of bicyclo(3.3.1)non-2-ene-9-one with diazomethane, a result he found surprising. However, he did not try an in situ reaction with diazomethane, ³⁵ which is usually the most effective condition for ring expansion reactions. ^{39,40} As a result of this failure, he turned instead to Tiffenau-Demjanov ring expansion of 9-aminomethyl-9-hydroxybicyclo(3.3.1)non-2-ene (33). This was made by forming the cyanohydrin of bicyclo(3.3.1)non-2-ene-9-one with potassium cyanide in ethanolic acetic acid. Since the cyanohydrin itself does not reduce with lithium aluminium hydride to the desired hydroxamine, but is converted to the parent ketone, it was first acetylated to 9-cyano-9-acetoxycyclo(3.3.1)non-2-ene (34), which is satisfactorily reduced with lithium aluminium hydride to the hydroxamine (33), which in turn satisfactorily underwent Tiffenau-Demjanov ring expansion to bicyclo(3.3.2)-2(3)-ene-9-one.

The overall yield was, however, at best only 36% from the starting material.

Apart from papers emanating from this group, there was, at the inception of this study, one other publication concerned with the chemistry of bicyclo(3.3.2)decane. This was an e.s.r. study of bicyclo(3.3.2)decane-9,10-semidione (35), by Russell.⁴¹ No synthetic details were given, other than that the semidione was made from diethyl cyclo-octane-1,5-dicarboxylate (36).⁴² Reference to other publications⁴³ from the same group indicate that the semidione is prepared by acyloin condensation of the diester (36) in the presence of trimethylsilylchloride to give O,O-bis(trimethylsilyl)bicyclo(3.3.2)dec-9-ene-9,10-diol (37), which is converted to the semidione by treatment with potassium tert.-butoxide in dimethylsulphoxide solution. Since this work was started several other publications dealing with bicyclo(3.3.2)decane chemistry have appeared. Both Leonard^{44,45} and Schleyer²⁹ have successfully ring expanded 9-bicyclo(3.3.1)nonanone (38) with methanolic diazomethane, and Leonard⁴⁵ has also applied this reaction successfully to bicyclo(3.3.1)non-2-ene-9-one (26). Chromic acid oxidation of the hydrocarbon gave the 1-bicyclo(3.3.2)decanol (14) described earlier, together with a small quantity of bicyclo(3.3.2)decane-1,5-diol (39). The bridgehead alcohol (14) was readily converted to 1-chlorobicyclo(3.3.2)decane (13), which was used in part of a study on bridgehead reactivities.⁴⁶ Leonard is interested in the manxane (bicyclo(3.3.3)undecane) system, and made several derivatives of bicyclo(3.3.2)decane in the course of a second ring expansion sequence.

Fig 2



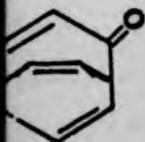
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Finally, Schmid,⁴⁷ has published a synthesis of bicyclo(3.3.2)decan-3,7,9-triene-2-one (40) as part of an elegant study of aromatic sigmatropic shifts. Heating cycloheptatrienyl propargyl ether gives the bicyclic compound (40) by a sequence of 1,5-hydride shifts, Claisen rearrangement, and internal ene-reaction (see fig. 2)

1,5 shift →

In spite of being so little studied, the bicyclo(3.3.2)decane system is very suitable for a number of reactivity studies, as well as posing interesting conformational problems. For some time studies into the mechanism of transannular hydride shifts have been proceeding in these laboratories, in order to try and answer some of the questions mentioned earlier, originally posed by Marvell.¹⁵ Our state of knowledge of the controlling factors in this field is still primitive, and the relative importance of those factors discussed by Marvell, as well as the molecular size of the reagent and reaction temperature has yet to be decided. Results so far from the 3-bicyclo(3.3.1)nonyl^{48,49} (41) and 3-bicyclo(3.3.2)decyl systems⁵⁰ (42) provide only a partial answer to the first two of Marvell's questions, namely the roles of proximity and ring strain. It was hoped that further studies on suitable bicyclo(3.3.2)decane derivatives and comparison of the results with analogous studies in related systems would shed more light on these questions. At the same time, Stevenson's^{50a} observation of a 2,6-hydride shift³⁵ in the bicyclo(3.3.1)nonane system, and Doyle's postulate of a



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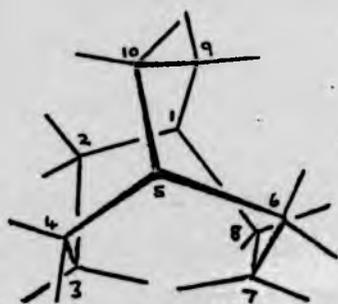
2,6-bridged twin-twist-boat carbonium ion being involved in the solvolysis of exo-2-bicyclo(3.3.2)decyl tosylate, prompted studies to determine whether a 2,6-hydride shift could in fact occur in the bicyclo(3.3.2)decane system.

Secondly, the results of Schleyer's ⁴⁶ bridgehead reactivity studies and our own observation of the ease with which even saturated bicyclo(3.3.2)decane derivatives undergo autoxidation prompted a study into autoxidation of bicyclo(3.3.2)decane as a synthetic method.

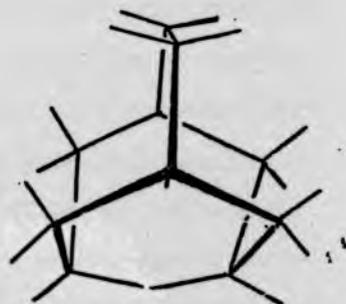
Thirdly, during the course of this work, a singular lack of reactivity on the part of 9-bicyclo(3.3.2)decanone was observed. This lack of reactivity, together with certain other observations that appear to be related, is discussed and rationalised in terms of Brown's I-strain theory.

Finally, there was in these laboratories a study into the single inversion Cope rearrangement. ^{51,52} It was apparent that bicyclo(3.3.2)deca-2,6-diene (10) would be an excellent compound for this study, which had been initiated by an examination of the thermal behaviour of bicyclo(3.3.1)nona-2,6-diene (43). ⁵³ No normal Cope rearrangement was observed in this system, but unfortunately, the single inversion Cope rearrangement is degenerate, and requires labelling techniques to detect its occurrence. The single inversion Cope rearrangement of bicyclo(3.3.2)deca-2,6-diene (10), however, is not degenerate, and so the synthesis of this compound was a further aim during this research.

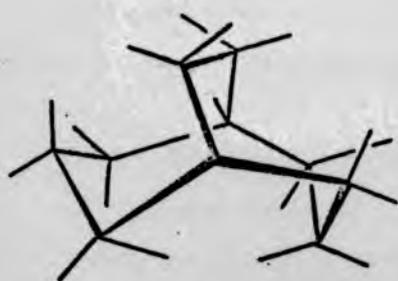
Fig 3



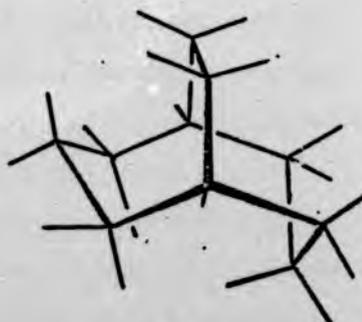
a.



b.



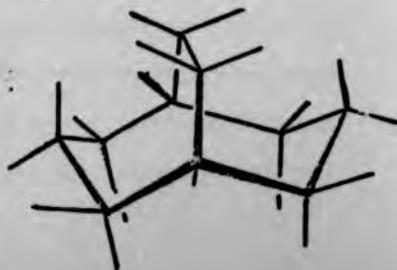
c.



d.



e.



f.

Turning now to
(3.3.2)decane system
illustrated in fig

a) The twin-
bridge at C9 and C10
action between the
separated by about
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b) The eclips
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at C9 and C10. Ag
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c) The stagger
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eclipsing strains
only results in the

of strain energy

Turning now to the conformational problems posed by the bicyclo (3.3.2)decane system, the six most likely conformations are illustrated in fig. 3 (a-f).

a) The twin-twist-chair. This has a staggered two carbon bridge at C9 and C10. There is a very serious transannular interaction between the endo C3 and C7 hydrogen atoms, which are separated by about 45 pm. (the van der Waals radius of a hydrogen atom is 120 pm.) with an associated C3...C7 distance of 215 pm. There are smaller interactions between C2 and C10, and C6 and C9. The serious C3-C7 interaction may be alleviated by flexing both rings outwards, thus incurring angle strain, which is energetically less expensive than a severe transannular interaction. (10° angle distortion C-C-C \cong 7.6 KJ mole⁻¹).⁵⁴ A Dreiding model of this conformation shows a considerable degree of flexibility.

b) The eclipsed-twin-chair. This has an untenable 3-7 interaction, the endo-hydrogens being separated by only 10 pm., with an associated C3...C7 distance of 210 pm. There is also torsional strain due to eclipsing on the two carbon bridge, and angle strain at C9 and C10. Again, the 3-7 interaction can be relieved by a flexing outward of the two rings.

a) The staggered boat-chair. This has two transannular interactions; between the hydrogens on C3 and C10 (80 pm.), and between the hydrogens on C4 and C7 (110 pm.). There are also partial eclipsing strains. Any attempt to relieve these strains by flexing only results in the creation of new strains.

d) The eclipsed boat-chair. This has the same eclipsed two carbon bridge and associated angle and torsional strains as (b). There are also smaller transannular interactions between the hydrogens on C3 and those on C6 and C8, and between C7 and those on C9 and C10.

e) The eclipsed-twin-boat. This has an apparently untenable combination of angle, torsional and transannular strain. A Dreiding model of this conformation spontaneously converts itself to (f).

f) The twin-twist-boat. This has a very serious transannular interaction between the endo hydrogens on C2 and C6. In addition, there are smaller interactions between the hydrogens on C3 and C9, and between C7 and C10. Lateral distortion alleviates the C2...C6 interaction at the expense of angle strain and increasing the weaker transannular interactions.

It is not clear which, if any, of these possible conformations is likely to be preferred in the majority of circumstances, and in September 1970 the evidence for any one rather than another was not overwhelming. Evidence from this group was in favour of a twin-chair conformation being generally preferred, ^{34,35} but Russell's e.s.r. study of bicyclo(3.3.2)decan-9,10-semidione, which showed that the semidione itself adopted a boat-chair conformation, was used as ⁴¹ evidence that this should be the generally preferred conformation. This discrepancy showed the necessity of further work in this field, while also suggesting that there may well be no one generally preferred conformation. This possibility is supported by the results ⁵⁵ of strain energy minimisation calculations by Schleyer on a series

of flexible bi- and tri-cyclic systems, including bicyclo(3.3.2)decane. These suggested that for such flexible molecules, there is often no unique geometry, but a number of conformations with closely similar energies. Rather, Schleyer suggests, in such flexible systems, conformation is determined largely by substituents rather than by the carbon skeleton.

The carrying out of such a conformational study also requires a considerable synthetic programme, and thus any synthetic entry to the bicyclo(3.3.2)decane system for these reactivity and conformational studies had to be capable of wide applicability. Of the syntheses already available, Alder's had been shown to be unsatisfactory. While bullvalene is a suitable precursor for several poly-substituted bicyclo(3.3.2)decane derivatives, as well as the parent hydrocarbon itself, its use as a starting material is effectively limited to those with a plentiful supply of cyclooctatetraene. However, bullvalene dibromide (4,8-dibromobicyclo(3.3.2)deca-2,6,9-triene (44)) promises to be the best precursor for bicyclo(3.3.2)deca-2,6-diene (10). Doyle's reexamination of Alder's work must also cast some doubt on the suitability of the Smith, Kline and French syntheses, since one route involves a somewhat similar deamination step, and another the intermediacy of a 6-bicyclo(3.2.2)nonylmethyl carbonium ion (45).

Thus the ring expansion of bicyclo(3.3.1)non-2-ene-9-one (26) was the only synthesis so far discovered that permitted selective substitution of the various positions in the bicyclo(3.3.2)decane ring.

Thus, the 9 position is already substituted, positions 2 and 3 (exo-configuration) can be substituted by hydroboration of bicyclo(3.3.2)decane (30) and the bridgeheads may be substituted by Schleyer's chromic and oxidation procedure. This synthetic route is thus suitable for derivatives substituted in only one of the seven membered rings, in spite of the rather poor overall yield. For derivatives substituted in both seven membered rings, however, there was no synthesis other than using bullvalene as a starting material.

This is in marked contrast to the bicyclo(3.3.1)nonane system, where there are many synthetic routes,^{56,57} with the possibility of almost any substitution pattern being easily incorporated. The reason for this striking difference is that the bicyclo(3.3.1)nonane ring is built of two linked cyclohexane rings, and is thus easily synthesised by aldol and Dieckmann type ring closures. By contrast, the thermodynamic instability of seven membered rings as compared with their open chain precursors makes seven membered rings difficult to synthesise by such ring closures,^{58,59} with the result that the bicyclo(3.3.2)decane system is correspondingly more difficult to synthesise.

It was with a view to carrying out the above described conformational and reacting studies that improved synthetic routes to the bicyclo(3.3.2)decane system were sought.

Chapter 1

Conformational Studies in the Bicyclo(3.3.2)decane System

Conformational Studies in the Bicyclo(3.3.2)decane System

As pointed out in the introduction, the bicyclo(3.3.2)decane system promised to be very suitable for a number of reactivity studies, particularly for the study of transannular hydride shifts.

However, in order to be able to make meaningful predictions and rationalisations regarding the reactivity of the system, a full conformational picture of the bicyclo(3.3.2)decane system is first required.

The six most likely conformations of the bicyclo(3.3.2)decane ring have already been discussed in the introduction. We may again summarize these conformations as follows; a twin-chair conformation in which the C9-C10 two-carbon bridge may be either eclipsed or staggered; a boat-chair conformation, which may again have either an eclipsed or a staggered two carbon bridge; and a twin-twist-boat conformation. A Dr-iding model of an extreme boat conformation is found to be mechanically unstable, and converts spontaneously to the twist-boat conformation. It has also been noted that there is evidence for both a twin-chair^{34,35} and a boat-chair⁴¹ conformation being generally preferred, while Schleyer,⁵⁵ as a result of strain energy minimisation calculations has suggested that conformation may well be determined primarily by the substituents in the ring, rather than the basic carbocyclic ring itself, though he finds that any twin boat conformation is $10.5 \text{ kJ mole}^{-1}$ less stable than either a twin-chair or a boat-chair.

It is relevant at this juncture to consider the conformational questions posed by two related ring systems; bicyclo(3.3.1)nonane (46) and tricyclo(4.3.1.1^{3.8})undecane (47) (homoadamantane). It is now accepted ⁶⁰ that the preferred conformation of bicyclo(3.3.1)nonane (46) is a distorted twin chair, the two ends of the molecule being splayed apart so as to relieve the strong transannular 3,7-interaction. Hence, one is unlikely to dismiss the possibility of bicyclo(3.3.2)decane also preferring a twin-chair conformation on the grounds of the unfavourable transannular 3,7-interaction demonstrated by a Dreiding model. Indeed, if the twin-chair conformation is in fact generally preferred for bicyclo(3.3.2)decane, the same conformational probes successfully used in the bicyclo(3.3.1)nonane series should be equally successful for bicyclo(3.3.2)decane.

By contrast, there is, as yet, no generally accepted picture for the homoadamantane skeleton. Here, the conformational question is whether the C4,C5 two carbon bridge is staggered or eclipsed, while the rest of the molecule is locked into a twin-chair. The factors governing the degree of stagger in the homoadamantane skeleton are likely to be similar to those in the bicyclo(3.3.2)decane system.

⁶¹ Schleyer and Nordlander ⁶² have both noted that the carbonyl stretching frequency of 4-homoadamantane (48) is 1698 cm.⁻¹ This corresponds to an expanded bond angle of 126° (see Chapter 2, section iii), which can be accounted for by an eclipsed bridge,

a staggered bridge could easily accommodate a normal bond angle of 120° .

61

Schleyer has also found evidence for an eclipsed bridge in the solution infra-red spectrum of cis-homoadamantane-4,5-diol (49), which shows a large intramolecular hydrogen bonding frequency shift ($\nu = 69 \text{ cm.}^{-1}$) from which he concludes that the diol possesses only a small dihedral angle, and that the preferred conformation in homoadamantane itself is therefore untwisted. However, the gain in energy resulting from the formation of an intramolecular hydrogen bond is often of the order of 21 kJ mole^{-1} ,⁶³ which is sufficient to exert a powerful influence on any one conformation relative to another.

64

Braun has performed an X-ray analysis on homoadamantane-4,5-dione (50), synthesised by Schlitzmann.⁶⁵ The dihedral angle between the two carbonyl groups was found to be 11.9° ; this result was interpreted by Schlitzmann as evidence for an almost fully eclipsed bridge in homoadamantane itself, on the grounds that the proximity of the two carbonyl groups should give rise to a strong dipole-dipole repulsion. Thus, unless there is a force constraining the two groups to an eclipsed conformation, the dihedral angle would be expected to be considerably larger than 11.9° .

Schleyer has also analysed the 220 Mc. NMR spectrum of homoadamantane⁶⁶; the protons of the two carbon bridge are reported to be equivalent, and to correspond to the A_4 part of an A_4X_2 system with $J_{AX} = 1.8 \text{ Hz.}$, which indicates a dihedral angle of about 60° between the bridgehead proton and the two bridge protons. The

a staggered bridge could easily accommodate a normal bond angle of 120° .

61

Schleyer has also found evidence for an eclipsed bridge in the solution infra-red spectrum of cis-homoadamantane-4,5-diol (49), which shows a large intramolecular hydrogen bonding frequency shift ($\Delta\nu = 89 \text{ cm.}^{-1}$) from which he concludes that the diol possesses only a small dihedral angle, and that the preferred conformation in homoadamantane itself is therefore untwisted. However, the gain in energy resulting from the formation of an intramolecular hydrogen bond is often of the order of 21 kJ mole^{-1} ,⁶³ which is sufficient to exert a powerful influence on any one conformation relative to another.

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equivalence must be due either to an eclipsed bridge or to rapid equilibration of the two extreme staggered conformations. Further, no temperature dependence such as would be expected to arise from a spectrum due to a rapid equilibrium could be detected, and so an eclipsed conformation was assigned to the two carbon bridge in homoadamantane. However, doubt has been cast on these assignments by Riddell⁶⁷, who considers that the coupling constant J_{AX} should in fact be 3.6 Hz., which corresponds to a much smaller dihedral angle. Riddell considers that the homoadamantane spectrum is deceptively simple.

In view of all this work, it is extremely interesting to note that the very recent X-ray determination of the structure of dimethyl homoadamantane-1,8-dicarboxylate (51) shows a dihedral angle of only 1°.⁶⁸

Finally, Schleyer's group have performed strain energy minimisation calculations on the homoadamantane skeleton, which originally predicted an eclipsed two carbon bridge;⁶⁹ but later calculations demonstrated the existence of a very broad energy minimum, indicating that there is no energy difference between a staggered and an eclipsed bridge in this system.⁵⁵ This could account for the equivalence of the bridge protons in the NMR being due to rapid equilibrium, while at the same time showing no temperature dependence.

Hence, it is by no means unlikely that the two carbon bridge in bicyclo(3.3.2)decane should also be eclipsed, and similar conformational probes should furnish information about the conformation of the two carbon bridge.

Returning to the bicyclo(3.3.1)nonane system, this was originally predicted by Eliel⁷⁰ and Whitham⁷¹ to prefer a boat-chair conformation, on the grounds that the transannular 3,7-interaction would render a twin-chair conformation unfavourable. In fact, the twin-chair conformation has been established for this ring system by a combination of solution infra-red data and X-ray analysis.⁶⁰

High frequency methylene stretching ($\nu(\text{C-H})$) bands had been noted⁷² in compounds where the molecular geometry resulted in severe steric crowding; for example, certain fused bicycloheptanes and half-cage structures. Given that steric crowding results in abnormally high frequency $\nu(\text{C-H})$ bands, a 3,7-interaction in the bicyclo(3.3.1)nonane ring would be expected to give rise to such bands, while any structural modification in the molecule which would alleviate any 3,7-interaction should result in the absence of these absorptions. de Vries and Ryason⁷² have examined the infra-red spectra of a series of compounds and attributed the observed high frequency stretching bands between 3055 and 2980 cm^{-1} to methylene crowding, and concluded that the hydrogen atoms of opposed methylene groups are vibrating in the presence of a repulsive field with a large component perpendicular to the direction of vibration, which would be expected, qualitatively, to raise the vibrational frequency.

Fig 1

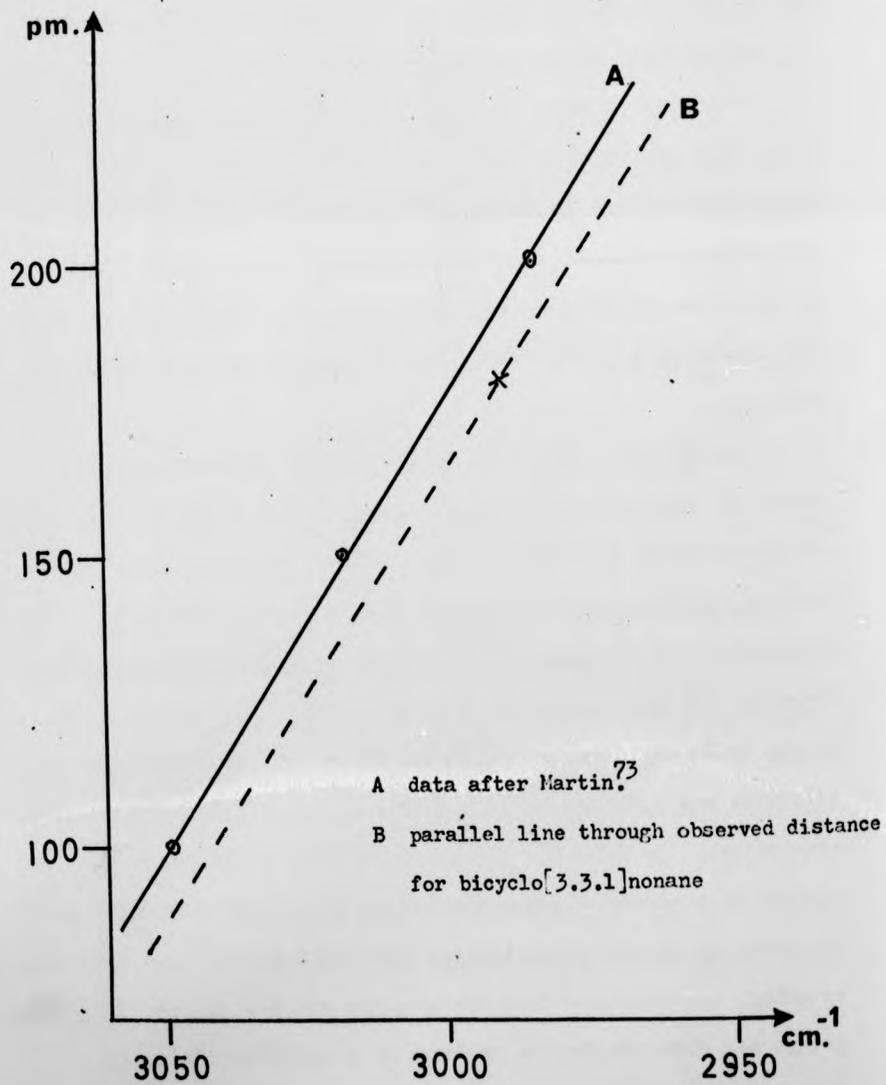
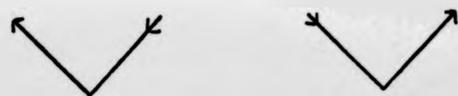


Fig 2a

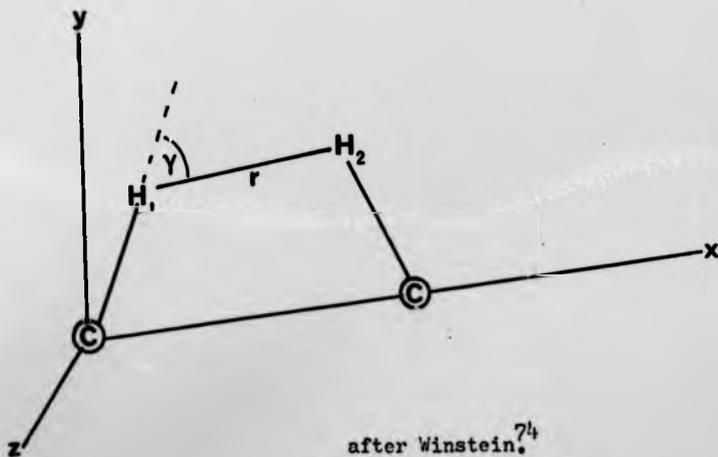


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Fig 2b



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Using molecular models, Martin⁷³ measured the distance separating the opposed atoms in α -nopinol and two fused ring compounds; all of which have a completely rigid carbon skeleton, and for which absorption frequency data had been quoted by de Vries and Ryason;⁷² and obtained a reasonable distance-frequency relationship from which inter-hydrogen distances could be deduced (see fig. 1).

⁷⁴Winstein also examined the increased $\nu(\text{C-H})$ frequencies in fused bicycloheptanes and half cage compounds, and showed that the four C-H bonds of the two interacting methylene groups couple in such a way as to produce only two stretching modes; symmetric-antisymmetric and anti-symmetric-antisymmetric (see fig. 2a). Winstein then developed a mathematical picture which indicated that the frequency shift is dependant on three factors (see fig. 2b):-

- 1) The angle γ between the C-H₁ bond and the line H₁...H₂. When γ is small, the non-bonding force is directed almost entirely along the C-H bond, and therefore has a maximum effect on the frequency shift.
- 2) The H₁...H₂ distance r . An increase in r results in lower frequency bands.
- 3) The force constants of the four bonds involved in the coupled vibrations; thus replacement of H by another moiety such as -OH or -D should alter the frequency shift.

Further, the theory indicated that unless the angle γ is close to 90° , the frequency shift in the symmetric-antisymmetric mode is very much greater than the shift in the antisymmetric-antisymmetric mode. The latter, however, would be expected to give rise to more

intense bands than the former, as the resultant dipole moment change will be greater for the latter mode. This agreed with the observed frequency shifts and intensities.

In the bicyclo(3.3.1)nonane system the $\nu(\text{C-H})$ region of the infra red spectrum is very complex, giving only a broad band envelope, even with very high resolution grating spectrophotometers. As a result, the only high frequency band which can be observed is the one due to the larger frequency shift, that is, the symmetric-antisymmetric mode, which is the weaker band. Further, because the frequency shift is smaller than those observed by Winstein, these bands are incompletely resolved, and are usually only visible as a shoulder on the high frequency side of the main envelope. However, examination of the methylene scissoring ($\delta(\text{C-H})$) bands also revealed high frequency absorptions which, though weak, were much better resolved than the $\nu(\text{C-H})$ bands.

⁷⁵
Chiurdoglu has classified the methylene scissoring absorptions of alicyclic ring hydrocarbons, ketones and alcohols ($\text{C}_5\text{-C}_{17}$) in terms of the number of distinct bands and the frequency differences between the highest and the lowest, intending to estimate the number of individually distinct types of methylene groups, and the degree of steric interaction present. Two conclusions were drawn from the work; (a) that the appearance of n bands in the $\delta(\text{C-H})$ region means that the molecule possesses at least n different types of CH_2 groups, and (b) the frequency difference between the highest and lowest bands was dependant on the degree of steric crowding, as the largest

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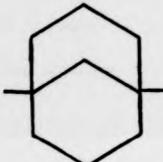
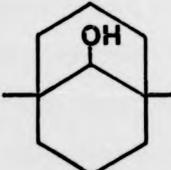
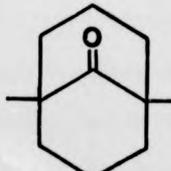
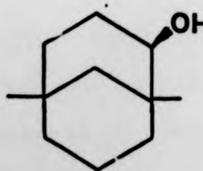


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Table 1

Abnormal $\delta(\text{C-H})$ bands for 1,5-dimethylbicyclo[3.3.1]nonanes.⁷⁶

	$\delta(\text{C-H}) \text{ cm.}^{-1}$	ϵ
 53	1488	20
 54	1490	45
 52	1490	45
 55	1488	45

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frequency differences were found for C₈, C₉ and C₁₀ rings. The first of these conclusions has been challenged by Dale¹⁹ who suggests that coupling can result in some bands being split into doublets. Since such a process appears to take place for the ν (C-H) bands discussed by Winstein, this seems not unlikely. Nonetheless, the second conclusion still seems perfectly justified and as a result, the high frequency δ (C-H) bands in the spectra of the bicyclo(3.3.1)nonane derivatives were also attributed to the steric interaction of the endo C3 and C7 hydrogens.

Hence, the compounds in table 1 were examined by Eglinton,⁷⁶ Martin and Parker; only those bicyclo(3.3.1)nonane derivatives in which a 3,7-transannular interaction could be present exhibited the high frequency ν (C-H) and δ (C-H) bands. Those compounds in which structural modification alleviated the interaction did not exhibit any anomalous absorptions. 3,9- and 7,9- Methylene interactions were ruled out as a possible cause of the abnormal ν (C-H) and δ (C-H) bands by the observation that 1,5-dimethyl bicyclo(3.3.1)nonane-9-one (52) did exhibit these bands. This compound could possess a 3,7-methylene interaction in a twin-chair conformation, but not a 3,9- or 7,9-methylene interaction in a boat-chair conformation. The infra red evidence was thus internally consistent with a twin chair conformation. To confirm that the C3 and C7 methylene groups were responsible for the bands at 2990 and 1490 cm.⁻¹, 2,3-dideutero-1,5-dimethyl-9-bicyclo(3.3.1)nonane (56) was synthesised; this compound exhibited a band at

1473 cm^{-1} of approximately 50% reduced intensity. Further confirmation for this assignment came from the work of Dale¹⁹ who found no bands at 2990 cm^{-1} in the spectra of 3,3-dideutro bicyclo(3.3.1)nonane (57) and 3,3,7,7-tetradeutrobicyclo(3.3.1)nonane (58).

The twin chair conformation being accepted, Martin⁷³ was able to calculate an approximate distance of 170 pm. for the separation between the endo hydrogens on C3 and C7 in bicyclo(3.3.1)nonane.

Finally, X-ray analysis of 1-(4-bromobenzenesulphonyloxy-methyl)-5-methyl-9-bicyclo(3.3.1)nonanol⁶⁰ (59) showed that this compound possessed a twin-chair conformation, with the 3,7-interaction alleviated by flexing the two rings outwards. Since this compound exhibited the characteristic abnormal absorption bands, both in the solid state and in solution spectra, extrapolation of the twin-chair conformation from the solid state to that in solution for all the compounds examined was possible, and the twin-chair conformation for the bicyclo(3.3.1)nonanes examined was taken as proven.

Since then, Webb and Becker⁷⁷ have examined the crystal structure of exo-2-chlorobicyclo(3.3.1)nonan-9-one (60); they found that the bond lengths and bond angles in this compound are almost identical with those observed for the brosylate (59), thus forming further evidence for the twin-chair conformation. The distance between the endo hydrogens on C3 and C7 is found to be

180 pm., in good agreement with Martin's estimate of 170 pm.

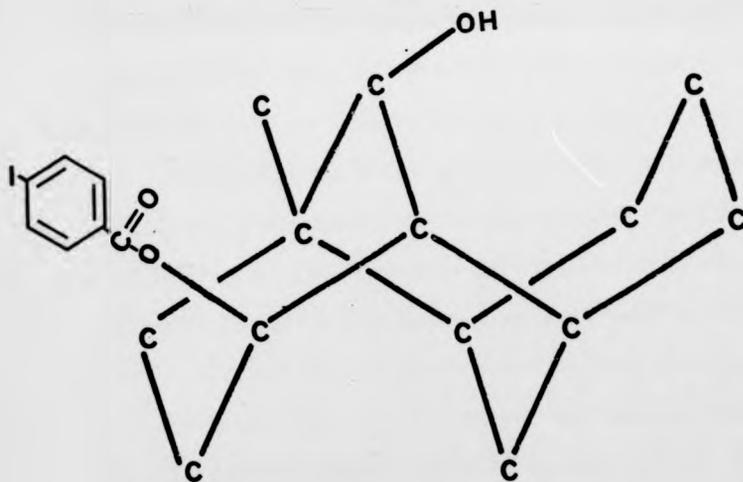
3-azabicyclo(3.3.1)nonane hydrobromide (61) has also been examined by X-ray analysis; again the conformation is a twin-chair and the interhydrogen distance is 180 pm.⁷⁸

Confirmatory evidence for the twin-chair conformation comes from the work of Pumphrey and Robinson⁷⁹ on the related tricyclo(7.3.1.0³⁷)tridecane system. In 5-tert.-butyl-anti-13-phenyl-syn-13-tricyclo(7.3.1.0³⁷)tridecanol (62), one of the two rings of the bicyclo(3.3.1)nonane moiety is locked in a chair conformation. If the other ring were in a boat, one of the hydrogens on C11 would be in the shielding zone of the benzene ring, and would therefore resonate at about 12 τ . The absence of any such signal in the NMR spectrum of this compound⁸⁰ indicates that the bicyclo(3.3.1)nonane moiety in fact prefers a twin-chair conformation. The same workers also examined the 3-azabicyclo(3.3.1)nonane system⁸¹; analysis of the NMR spectra of 7-tert.-butyl-3-azabicyclo(3.3.1)nonane (63) and its N-methyl derivative (64), showed a twin-chair conformation to be present in this ring system also, though here the endo-3-hydrogen is replaced by the lone pair on the nitrogen, thus indicating that the conformational requirement of a lone pair of electrons is less than that of a hydrogen atom, contrary to the current belief at that time.

A further interesting and relevant result comes from Macrossan's study of the tricyclo(5.3.1.1^{2,6})dodecane system, which could

Fig 3

Conformation of tricyclo[5.3.1.1^{2,6}]dodecane.



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As a result of these various researches, it is now accepted that the bicyclo(3.3.1)nonane system exists preferentially in a twin-chair conformation, unless such a conformation is totally impossible, for example if there is a bulky endo-3-substituent.

The success of a combination of infra-red spectroscopic and X-ray crystallographic techniques in solving the conformational problem for the bicyclo(3.3.1)nonane system suggested that some information regarding the preferred ground state conformation of bicyclo(3.3.2)decane might also be successfully gained by these means. Certainly one would expect that any bicyclo(3.3.2)decane derivative which adopts a twin-chair conformation should exhibit abnormal ν (C-H) and δ (C-H) bands provided that the molecular geometry does not rule out a 3,7-interaction. Doyle³⁵ examined the high resolution infra-red spectra of several substituted bicyclo(3.3.2)decanes, and found abnormal methylene scissoring bands (δ (C-H)) for several compounds, all of which would possess a 3,7-transannular interaction in a twin-chair conformation. Other compounds, in which

ane.
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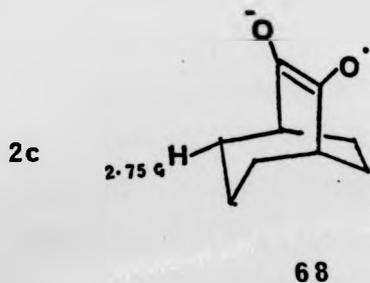
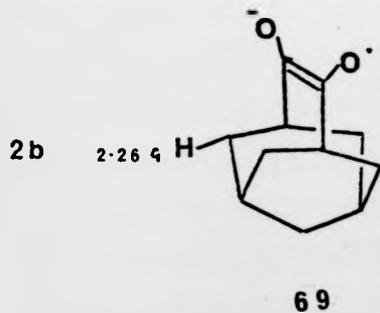
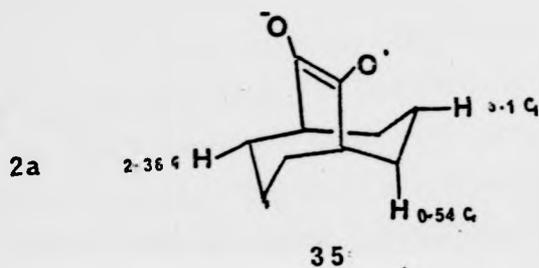
the molecular geometry was such as to alleviate any 3,7-interaction, did not exhibit any abnormal bands.

This preliminary examination of solution infra-red spectre of bicyclo(3.3.2)decane derivatives was carried out because there was evidence for a twin-chair conformation for exo-3-bicyclo(3.3.2)decanol (3) in its NMR spectrum. The exo configuration for this alcohol was originally assumed from the synthesis, by hydroboration of 2-bicyclo(3.3.2)decene (30). Hydroboration is known to occur stereoselectively from the less hindered side of a double bond, and examination of molecular models suggests that for 2-bicyclo(3.3.2)decene (30), the less hindered face is exo to the two carbon bridge. While this does not constitute proof that the alcohol (3) does in fact have the exo-configuration, it suggests that it is extremely likely; and further evidence comes from the NMR spectrum. The C3 carbonyl proton is observed to resonate at 5.7 τ and it is a strongly coupled multiplet. The strengths of the couplings (11 Hz. and 5 Hz.) are only consistent with this proton being an axial proton, the 11 Hz. coupling being to the axial protons on C2 and C4 and the 5 Hz. coupling being to the equatorial protons. If this proton is axial, the hydroxyl group must be equatorial, therefore it must be either an exo-3-hydroxyl group, with the bicyclo(3.3.2)decane ring in a chair conformation (66), or it must be an endo-3-hydroxyl group, attached to the boat part of a boat-chair conformation. The exo-configuration, and concurrently, the twin-chair

conformation, is established by the field position of the carbonyl proton resonance. Since cycloheptanol is observed to resonate at 6.16 τ ,³⁵ in the 3-bicyclo(3.3.2)decanol under discussion the carbonyl proton is appreciably deshielded. The deshielding mechanism must be transannular, and is therefore due to the endo-7-proton in a twin-chair conformation (66) or to the syn-9- and syn-10-protons in a boat-chair conformation (67). In fact the degree of deshielding is similar to that observed in exo-3-bicyclo(3.3.1)nonanol (29) which must exist as a twin-chair; in this case the C3 carbonyl proton resonates at 5.68 τ ³⁸ while the carbonyl proton in cyclohexanol is found between 6.0 and 6.7 τ .⁶⁷ As the carbonyl proton for exo-3-bicyclo(3.2.1)octanol (where no transannular deshielding is possible) resonates at 6.25 τ ,⁸⁸ the unusually low field position of the signal in the bicyclo(3.3.1)nonanols was ascribed to transannular deshielding of the endo-carbonyl proton by the endo-hydrogen on C7 in a twin-chair conformation. Hence, the equally abnormal low field position for the carbonyl proton in exo-3-bicyclo(3.3.2)decanol (3) must be due to the same transannular deshielding mechanism, and therefore the exo-configuration in a twin-chair conformation is established.

However, Russell's e.s.r. study of bicyclo(3.3.2)decane-9,10-sepidione (35) and bicyclo(3.2.2)nonane-6,7-sepidione (68) was interpreted as suggesting that bicyclo(3.3.2)decane itself prefers a boat-chair conformation. The pertinent data, as well as those for homoadamantane-4,5-sepidione (69), are displayed in table 2. Russell had already shown that β -hydrogens with a trans-coplanar

Table 2



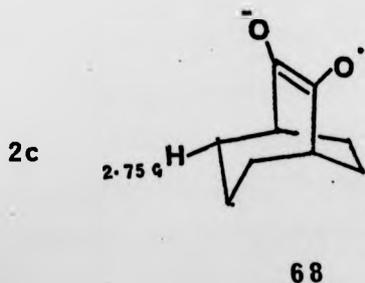
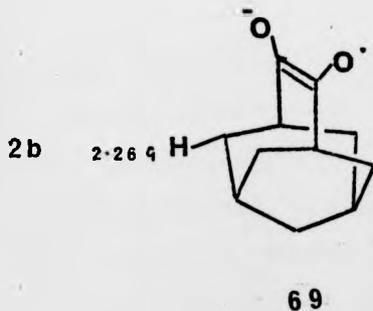
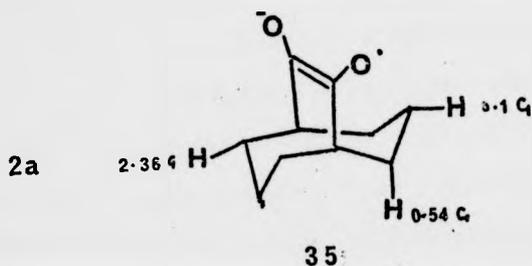
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arrangement of bonds to the carbon F_z orbital of the π -system have large hyperfine splittings (1.8-2.6G) when a seven membered ring is in a chair form, while when the seven membered ring is in a boat, the splittings are reduced to about 0.5G.

If bicyclo(3.3.2)decane-9,10-semidione (35) existed as a twin-chair, its e.s.r. spectrum would be similar to that of the homoadamantane analogue (69), which is a quintet, showing four large splittings corresponding to the four equatorial β -hydrogens (2b).

In fact, the spectrum is a triplet of triplets, corresponding to 2 large splittings (2.36G) resulting from 2 equatorial β -hydrogens and 2 small splittings (0.54G) resulting from 2 axial β -hydrogens (2a). A twin-boat conformation would have no large couplings, and thus would result in a spectrum which is a quintet, with four small splittings due to four axial β -hydrogens. Further, the observed spectrum exhibits small doublet splittings of 0.1G. These must arise by long range coupling from the γ -hydrogens, only a boat-chair conformation could give rise to doublet splittings. Thus a boat-chair conformation is established for bicyclo(3.3.2)decane-9,10-semidione (35), and as a concomitant, for 9-bicyclo(3.3.2)decene (70).

In order to relate this result to the conformation of bicyclo(3.3.2)decane itself, Russell then examined the e.s.r. spectrum of bicyclo(3.2.2)nonane-6,7-semidione (63), in order to determine the

relative preferences of saturated and unsaturated seven membered rings for the chair form. The ambient temperature spectrum indicated rapid ring flipping, but at -65° , a spectrum corresponding to a conformation with the double bond in a chair was frozen out (20).

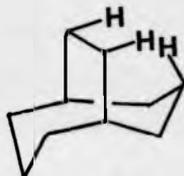
Russell then argues thus:- the seven membered ring containing the semidione group prefers the chair conformation to a slightly greater extent than does the saturated seven membered ring. Relating this to bicyclo(3.3.2)decane-9,10-semidione (35), it would seem that this would have a greater preference for a twin-chair conformation than bicyclo(3.3.2)decane (1) itself. Since in fact the semidione exists as a boat-chair, bicyclo(3.3.2)decane itself must exist as a boat-chair. This argument seems unsatisfactory, to say the least. The transposition of the conformational preference of flexible molecular segments from one ring system to another without consideration of the molecule in question as a whole can often lead to erroneous conclusions.

Accepting the clear result that bicyclo(3.3.2)decane-9,10-semidione (35) exists as a boat-chair, it was decided to look at systems with an unsaturated two carbon bridge more closely. A Dreiding model of 9-bicyclo(3.3.2)decane (70) showed that the double bond greatly restricted the flexibility of the ring system as a whole, by constraining C1, C9, C10 and C5 to be coplanar, while in a twin-chair conformation (71) also greatly increasing the interaction between the endo hydrogens on C3 and C7. In other words,

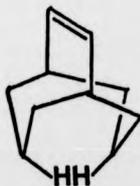
Fig 4



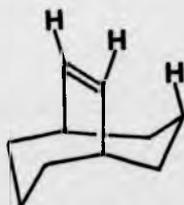
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70

compared with the parent
strain is increased when
flexing is reduced. How
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At this stage it is
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compared with the parent saturated hydrocarbon (72), the transannular strain is increased while the opportunity for its relief by ring flexing is reduced. However, in a boat-chair conformation, the interaction between hydrogens on C9 and C10 with those on C3 is much reduced in 9-bicyclo(3.3.2)decene (70) as compared with bicyclo(3.3.2)decane (73) itself. Thus, it is not at all unreasonable that bicyclo(3.3.2)decane derivatives with a double bond at position 9 should prefer a boat-chair conformation, while those derivatives with a saturated two carbon bridge may well still prefer a twin-chair conformation (see fig. 4).

At this stage it is relevant to consider in detail Schleyer's⁵⁵ strain energy minimisation calculations for possible conformations of bicyclo(3.3.2)decane. He finds that both the boat-chair and the twin-boat conformations exhibit broad energy minima, in other words, there is no energy difference between a boat-chair conformation with the bridge eclipsed, and one with the bridge staggered. The same applies for the twin-boat, contrary to the prediction of Dreiding models (see introduction). For the twin-chair conformation, however, Schleyer finds that a staggered two carbon bridge, with a dihedral angle of 22° to be some 10 kJ mole^{-1} more stable than the form with an eclipsed two-carbon bridge. It is considered that this is due to the stagger relieving the 3,7-non-bonded interaction, and Schleyer feels that the very broad energy minimum found for homoadamantane, where the twin-chair is

locked by a methylene bridge which also removes the non-bonded interaction, is strong supporting evidence for this explanation of the rigidity of the staggered twin-chair conformation. In absolute terms, it is found that the staggered twin-chair and the boat-chair conformations are all of equal energy, while the twin-boat conformations are some $10.5 \text{ kJ mole}^{-1}$ less stable. Schleyer then concludes that for the bicyclo(3.3.2)decane system, the preferred conformation will be determined mainly by the substituents present rather than the ring system itself.

Before we can take such calculations at face value, though, we need to know how reliable they are. The first thing that must be appreciated is that such calculations are semi-empirical; therefore the result depends on the quality and the applicability of the experimental data used. Hence, while such calculations offer very useful guidelines, they are not a complete conformational analysis, and they are no substitute for actual measurements on individual compounds.

We have thus seen, at the commencement of this project, that there was compelling evidence for a twin-chair conformation for exo-3-bicyclo(3.3.2)decanol (3), and for a boat-chair conformation for bicyclo(3.3.2)decane-9,10-semidione (37). Further, infra-red spectral data had indicated that a twin-chair conformation might well be more generally preferred, while extrapolation of the data from the semidione study had suggested that a boat-chair was in

fact generally preferred. Finally, the results of theoretical calculations published since this study was begun suggest that there may well be no one preferred conformation.

The first task was the synthesis of several compounds which would be predicted to exhibit anomalously high frequency ν (C-H) and δ (C-H) bands. At the same time, it was essential to prepare 9-bicyclo(3.3.2)decene (70) which was expected to exist as a boat-chair, and thus not exhibit anomalous bands in the infra-red. A further compound of particular interest was bicyclo(3.3.2)decane-9,10-dione (74), which, if it exhibited anomalous scissoring and stretching bands, proved that they were not due to interactions between the hydrogens on C3 and C9 or C10 in a boat-chair; while it was also expected to shed some light on the question of whether or not the two carbon bridge is staggered, as was done for the homo-adamantane-4,5-dione (50).

9-Bicyclo(3.3.1)nonanone (38), prepared from cyclo-octa-1,5-diene and nickel tetracarbonyl⁹⁰ was reacted with diazomethane as described by Leonard,⁴⁴ or Schleyer²⁹ to give 9-bicyclo(3.3.2)decanone (75) which satisfactorily underwent Wolff-Kisher reduction to bicyclo(3.3.2)decane (1). Reduction of 9-bicyclo(3.3.2)decanone (75) to 9-bicyclo(3.3.2)decanol (24) initially proved troublesome, in that borohydride reduction gave only a 20% yield of the required alcohol, and catalytic methods failed completely. However, lithium aluminium hydride reduction was ultimately found to reduce 9-bicyclo(3.3.2)decanone in excellent yield. (For a fuller discussion of this, and related questions, see chapter 2, section (iii)). Subsequent treatment of the alcohol with ethyl chloroformate in

pyridine furnished the crude mixed carbonate ester which was pyrolysed to give 9-bicyclo(3.3.2)decene (70) in acceptable yield.

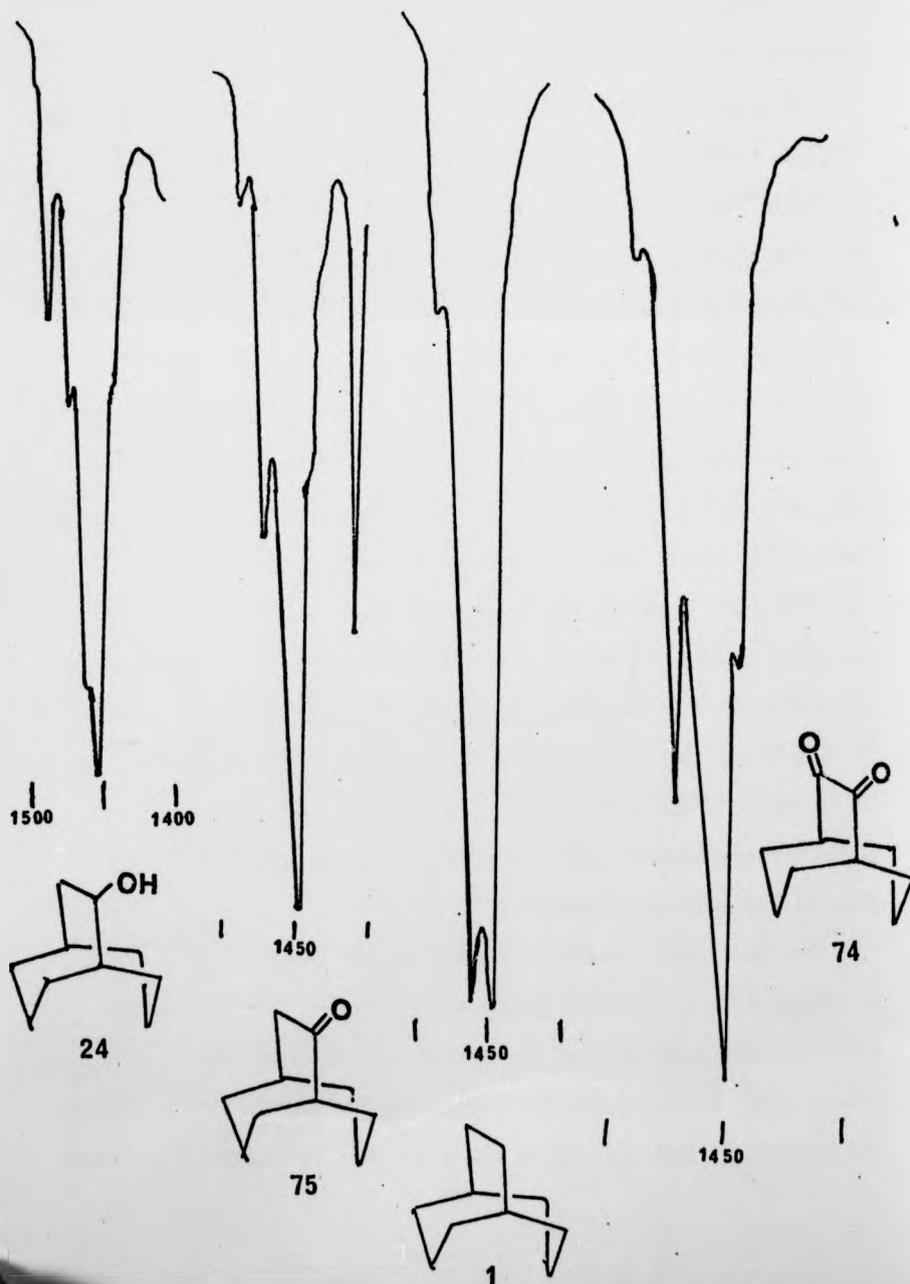
Finally, selenium dioxide oxidation of 9-bicyclo(3.3.2)decanone furnished bicyclo(3.3.2)decan-9,10-dione (74) as bright yellow crystals. Condensation of the dione (74) with *o*-phenylene diamine gave the corresponding quinoxaline, 7,8,9,10-tetrahydro-6,10-propano cyclohepta(b)quinoxaline (75).

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Subsequent to this work, Schleyer published details of a synthesis of 9-bicyclo(3.3.2)decene (70), by elimination of tosylate from 9-bicyclo(3.3.2)decyl tosylate (77) in dimethyl sulphoxide with potassium tert.-butoxide. This reaction was reported to give much better yields than the carbonate pyrolysis, and so was investigated. However, GLC analysis of the product on a NEP 50m. capillary column showed the presence of variable and usually minor quantities of a by-product. On one occasion, though, the quantity of by-product was equal to that of the 9-bicyclo(3.3.2)decene. The by-product has not been isolated; however the NMR spectrum of the 50:50 mixture showed complex olefinic absorption at higher field than in 9-bicyclo(3.3.2)decene.

The same paper contained details of the synthesis of a mixture of 1-bicyclo(3.3.2)decanol (14) and bicyclo(3.3.2)decan-1,5-diol (39), and the conversion of the former to 1-chlorobicyclo(3.3.2)decane (13). Adjustment of the conditions for chromic acid oxidation of bicyclo(3.3.2)decene led to the development of suitable syntheses

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for either the bridgehead alcohol (14) and the bridgehead diol (39). Thus treatment of bicyclo(3.3.2)decane with chromium trioxide in solution in acetic acid and acetic anhydride for three quarters of an hour gave, after reduction of the intermediate acetate with lithium aluminium hydride, 1-bicyclo(3.3.2)decanol (14) and a small quantity of unreacted hydrocarbon. The use of larger quantities of chromium trioxide, longer reaction time and higher reaction temperature gave an acceptable yield of bicyclo(3.3.2)decan-1,5-diol (39). Treatment of the bridgehead alcohol (14) with thionyl chloride as described by Schleyer²⁹ gave 1-chloro-bicyclo(3.3.2)decane (13), while a suspension of the bridgehead diol (39) in a methylene chloride:thionyl chloride mixture gave 1,5-dichloro bicyclo(3.3.2)decane (78).

All these compounds, apart from 9-bicyclo(3.3.2)decene (70) and the quinoxaline (76) were predicted to exhibit bands in the infra-red at approximately 2980 and 1485 cm^{-1} . Such bands were in fact observed, and the data is collected in table 3 (below). Examples of relevant spectra are reproduced as fig. 5. The quinoxaline (76) and 9-bicyclo(3.3.2)decene, having rigid double bonds in the two carbon bridge were predicted to exist preferentially in a boat-chair conformation, and so not exhibit any bands at 2980 cm^{-1} and 1485 cm^{-1} . In the event, neither exhibited a band at 2980 cm^{-1} , while the region immediately below 1500 cm^{-1} was obscured by strong aromatic bending bands in the spectrum of the quinoxaline (76); 9-bicyclo(3.3.2)decene (70), however, exhibits a very weak shoulder at 1485 cm^{-1} in solutions of very high



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concentration. In solid state spectra this shoulder is absent. This could be due to a conformational mixture being present in solution, a small quantity of twin-chair conformer giving rise to a very weak high frequency scissoring band; whereas, in the solid state, only the preferred boat-chair conformer would be present.

Attention now turned to compounds substituted at positions 2 and 3. Doyle had already shown that ring expansion of bicyclo(3.3.1)non-2-ene-9-one (26) to bicyclo(3.3.2)dec-2(3)-ene-9-one (31 and 32), followed by Wolff-Kishner reductions of the ketone mixture gave 2-bicyclo(3.3.2)decene³⁵ (30). Neither of these compounds exhibited bands at 2980 or 1465 cm^{-1} in their infra-red spectra, as predicted, as in these compounds there can be no 3,7-interaction. However, as stated in the introduction, the yield by Doyle's synthesis was at best only 36%. Further, the use of large quantities of cyanide and the comparative slowness of a several step synthesis were also disadvantages.

Successful ring expansion of the saturated 9-bicyclo(3.3.1)^{39,29}nonanone (38) using diazomethane prepared in situ in methanol suggested that this method might also be suitable for the ring expansion of the unsaturated bicyclo(3.3.1)non-2-ene-9-one (26), as Doyle's attempt at direct homologation of this material with diazomethane had been carried out in ether solution, using a lithium chloride catalyst.

The advantage of using in situ diazomethane in methanol is

that methanol is a powerful catalyst for the addition of diazomethane to ketones; further, the method is considerably safer than the ex situ mode of reaction in ether on a large scale, as there is no distillation involved, nor is there a large quantity of diazomethane present at any one time. In the event, bicyclo(3.3.1)non-2-ene-9-one (26) did react with diazomethane in methanol, but gave a mixture of the desired bicyclo(3.3.2)dec-2(3)-ene-9-one (31 and 32) and 9-epoxymethylenebicyclo(3.3.1)non-2-ene (79). The reaction product was treated with potassium hydroxide in aqueous ethanol to destroy the large quantity of methyl tosylate produced in the in situ reaction. This resulted in opening of the exocyclic epoxide to an aldehyde group, furnishing bicyclo(3.3.1)non-2-ene-9-carboxaldehyde (80), which was separated from the required bicyclo(3.3.2)dec-2(3)-ene-9-one (31 and 32) by chromatography on alumina. While this method was quicker than Doyle's, and gave better yields, separation of the by product was tedious. The question of why the saturated 9-bicyclo(3.3.1)nonanone (38) gives no exocyclic epoxide, while the unsaturated bicyclo(3.3.1)non-2-ene-9-one (26) does, is discussed, together with the related questions, in chapter 2, section (iii).

The method of choice for the ring expansion of bicyclo(3.3.1)non-2-ene-9-one (26) is based on the work of Mock and ⁹¹Hartmann who discovered a synthesis of β -Keto esters from ketones

containing one less carbon atom, using ethyl diazoacetate with triethylxonium fluoroborate as catalyst. For example, cyclohexanone reacts with ethyldiazoacetate to give 2-carbethoxycycloheptanone in 90% yield. Since this reaction is also a ring expansion procedure, we decided to investigate its applicability to our system. Exocyclic epoxides (in the form of glycollic esters) were found by Mock and Hartmann only as very minor products; only one ring expansion step took place. Normally, the β -keto ester is separated from excess ethyl diazoacetate and any glycollic esters by distillation. However, our interest lay in the ring expanded ketone rather than the β -keto ester, hence a hydrolysis and decarboxylation step was necessary. Treatment with methanolic potassium hydroxide was expected to convert excess ethyl diazoacetate and any glycollic esters to water soluble salts during the hydrolysis and decarboxylation procedure, thus simplifying the purification. In the event, bicyclo(3.3.1)non-2-ene-9-one was found to react readily with ethyl diazoacetate in the presence of triethyl-oxonium fluoroborate. The crude reaction product was treated with refluxing methanolic potassium hydroxide solution, to give pure bicyclo(3.3.2)dec-2(3)-ene-9-one (31 and 32) in 60% yield. The two compounds in the mixture were found to be present in equal quantities by GLC analysis on a 50' carbowax column, and they could be separated by chromatography on alumina. Wolff-Kishner reduction of the ketone mixture gave 2-bicyclo(3.3.2)decene (30), which was epoxidised with *m*-chloroper-

benzoic acid in methylene chloride. The product was shown to be the expected exo-2,3-epoxybicyclo(3.3.2)decane (31) by reduction with lithium aluminium hydride to exo-2-bicyclo(3.3.2)decanol (5), identical with a sample prepared by Doyle. Hydroboration of 2-bicyclo(3.3.2)decene (30) gave a mixture of exo-2- (5) and exo-3-bicyclo(3.3.2)decanol (3), in the ratio 35:65. An attempt to increase the yield of exo-3-bicyclo(3.3.2)decanol (3) by using disiamylborane was not significantly successful, giving 70% instead of 65%. The two alcohols could be separated by chromatography on alumina, and from the alcohols the corresponding ketones were obtained by oxidation of an ethereal solution of the alcohol with Jones' chromic acid. The use of ether as solvent for these oxidations was adopted after difficulties had been experienced when oxidising unsaturated alcohols to unsaturated ketones in acetone solution. (See chapter 2, section (1)). Use of ether as solvent also greatly facilitates work up of the reaction, since excess reagent and inorganic material can be removed by treatment with granular anhydrous potassium carbonate, which is easily filtered off, leaving a dry ethereal solution of the required ketone.

The high resolution infra-red spectra of all these compounds were carefully examined. Only exo-2-bicyclo(3.3.2)decanol (5) showed a band at 1485 cm.^{-1} , and then only a weak shoulder. While none of bicyclo(3.3.2)dec-2(3)-ene-9-one (31 and 32), 2-bicyclo

(3.3.2)decene (30), exo-2,3-epoxybicyclo(3.3.2)decane (31) and 3-bicyclo(3.3.1)decanone (82) would be expected to exhibit abnormal $\nu(\text{C-H})$ and $\delta(\text{C-H})$ bands, it would not be unreasonable to expect exo-3-bicyclo(3.3.2)decanol (3) and 2-bicyclo(3.3.2)decanone (83) to absorb at 2960 and 1465 cm.^{-1} . For the 2-ketone (83), however, inclusion of a trigonal centre in the ring will certainly alter the ring geometry somewhat, and will almost certainly result in a greater splaying apart of C3 and C7, with the result that the scissoring band will be of lower frequency, and thus masked by the other methylene absorptions. It is also possible that in this case we do in fact have a boat-chair conformation (ketone in boat, 84) as has been suggested by Marvell⁹⁴ for the analogous 2-bicyclo(3.3.1)nonanone (85 and 86).

In the case of exo-3-bicyclo(3.3.2)decanol (3), the absence of any abnormal bands is also not entirely unexpected, as the corresponding exo-3-bicyclo(3.3.1)nonanol (29) also has no such bands, in spite of a twin-chair conformation having been clearly demonstrated for both alcohols by NMR. The explanation is forthcoming from Winstein's theoretical picture⁷⁴; since the frequency of abnormal $\nu(\text{C-H})$ bands depends on the force constants of the bonds involved, replacement of even one of the four hydrogens on C3 and C7 should result in a frequency shift of the abnormal $\nu(\text{C-H})$ band, and one would expect the same to be true for the $\delta(\text{C-H})$ bands. In other words, the absence of any abnormal bands in the infra-red spectrum of exo-3-

bicyclo(3.3.2)decanol (3) is evidence that the abnormal bands observed in other compounds are, in fact, due to a specific 3,7-interaction. As a final check on this, it was decided to synthesise 3,3-dideuterobicyclo(3.3.2)decane (87) which would not be expected to exhibit any abnormal bands in its infra-red spectrum (c.f. Dale's studies of 3,3-dideuterobicyclo(3.3.1)nonane (57) and 3,3,7,7-tetradeuterobicyclo(3.3.1)nonane (58)¹⁹) and 2,2-dideuterobicyclo(3.3.2)decane (88), which should exhibit the abnormal bands. Reduction of 3-bicyclo(3.3.2)decanone (82) with lithium aluminium deuteride to a mixture of exo-3- and endo-3-deutero-3-bicyclo(3.3.2)decanols (89 and 90), followed by tosylation and reduction of the mixed tosylates with lithium aluminium deuteride gave a mixture of 3,3-dideuterobicyclo(3.3.2)decane (87) and 3-deutero-2-bicyclo(3.3.2)decene (91) in a ratio of 40:60. The saturated hydrocarbon was separated by preparative layer chromatography on 25% silver nitrate-silica gel. 2,2-Dideuterobicyclo(3.3.2)decane (88) was prepared by an identical method, starting from 2-bicyclo(3.3.2)decanone (83). A similar ratio of olefin to saturated hydrocarbon was obtained.

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Since these syntheses were carried out, Brown has reported that lithium triethylborohydride is an extremely powerful nucleophile, and in reactions with cycloalkyl halides gives no elimination products; even exo-2-bromonorbornane (92), which is highly resistant

to δ^2 substitution, is quantitatively reduced to norbornane at 65°. Since lithium triethylborodeuteride is available from lithium deuteride and triethylborane, this reagent will be the reagent of choice for future syntheses of deuterated bicyclo(3.3.2)decane derivatives.

As predicted, 3,3-dideuterobicyclo(3.3.2)decane (87) did not exhibit any abnormal $\nu(\text{C-H})$ or $\delta(\text{C-H})$ bands, while 2,2-dideuterobicyclo(3.3.2)decane (88) does exhibit the bands, though they are much weaker than in bicyclo(3.3.2)decane itself. The reason for this is not clear, but it is probably related to the observed very weak 1485 cm.^{-1} band in exo-2-bicyclo(3.3.2)decanol (5). It appears that any kind of substitution at position 2 affects the coupled vibrations of the hydrogens at position 3 and position 7 in such a manner as to reduce the intensity of the bands.

Nevertheless, these observations of a total absence of abnormal bands in exo-3-bicyclo(3.3.2)decanol (3) and 3,3-dideuterobicyclo(3.3.2)decane (87), and the presence of these bands, though weak, in exo-2-bicyclo(3.3.2)decanol (5) and 2,2-dideuterobicyclo(3.3.2)decane (88) prove conclusively that these abnormal bands arise from the hydrogen atoms on C3 (and C7). Since the bands are also present in the spectra of bicyclo(3.3.2)deca-9,10-dione (74) and 9-oxa-10-bicyclo(3.3.2)decanone (93),⁹⁶ they cannot be due to interactions between hydrogens on C3 (or C7) and those on C9 and C10 in a boat-chair conformation; thus they must be due to a 3,7-interaction

in a twin-chair conformation. These results also exclude the possibility of these bands being due to a 2,6-interaction in a twin-twist-boat conformation which has been suggested⁹⁷ as a possible, though unlikely, cause of these bands in the bicyclo(3.3.2)decane system. If these bands had in fact arisen from a twin-twist-boat conformation, one would have expected exo-3-bicyclo(3.3.2)decanol (3) to have exhibited abnormal bands instead of exo-2-bicyclo(3.3.2)decanol (5).

The frequency of the abnormal bands in the bicyclo(3.3.2)decane are 2980 cm.^{-1} and 1485 cm.^{-1} as compared with 2990 cm.^{-1} and 1490 cm.^{-1} for bicyclo(3.3.1)nonane. This shows that the interhydrogen distance is greater for bicyclo(3.3.2)decane; and from the figure 2980 cm.^{-1} this may be estimated as $200 \pm 20\text{ pm.}$, using the graph in fig. 1.

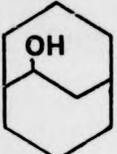
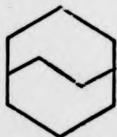
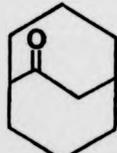
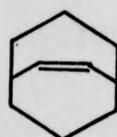
The significance of this result is that Dreiding models predict a smaller interhydrogen distance for bicyclo(3.3.2)decane than for bicyclo(3.3.1)nonane. This suggests that the two carbon bridge greatly increases the flexibility of the overall ring system as compared with bicyclo(3.3.1)nonane; this is an important factor from both the conformational point of view and when considering the reactivity of the system.

Thus, we see that the abnormal bands in the infra-red spectra of bicyclo(3.3.2)decane derivatives are consistent with, and only with, a twin-chair conformation existing in solution. However, the

Table 3a

Abnormal $\nu(\text{C-H})$ and $\delta(\text{C-H})$ and extinction coefficients for
9- and 10- substituted bicyclo[3.3.2]decane derivatives.

Solutions in carbon tetrachloride, 1 mm. path length.

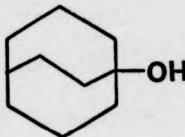
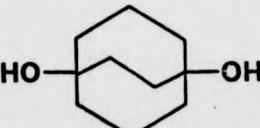
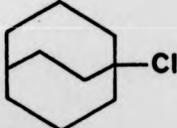
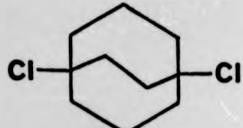
	$\nu(\text{C-H})$	$\delta(\text{C-H})$	A	[c]	ϵ_{δ}
 24	2982	1486	0.14	0.065M	22
 1	2980(sh)	1485	0.23 ⁺	0.362M ⁺	13
 75	2981(sh)	1485	0.08	0.129M	6.5
 74	2980(sh)	1485	0.0081 ⁺	0.018M ⁺	4 [*]
 70	NONE	1485(sh)	0.0183	0.0675M	2 [*]

* weak bands, ϵ is only approximate

+ calculated from data at other concentrations.

Table 3b

Abnormal bands in bridgehead substituted bicyclo[3.3.2]decanes.

	$\delta(\text{C-H})$	$\nu(\text{C-H})$
 14	1486	2989
 39	1484(KBr) not observable in solution	2979(KBr) 2982(CDCl ₃)
 13	1484	2983
 78	1485	2982

evidence does not
 The possibility of a
 for 9-bicyclo(3.3.2)
 taken together with
 chair and twin-chair
 possibility of a con
 other bicyclo(3.3.2)
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 indeed be the case.

If we look at t
 and 1485 cm.⁻¹ for t
 decrease in intensit
 decane (1) > 9-bicyclo
 9,10-dione (74) > 9-
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 head alcohol (14) is
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2]decanes.

v(C-H)

2989

2979(KBr)

2982(CDCl₃)

2983

2982

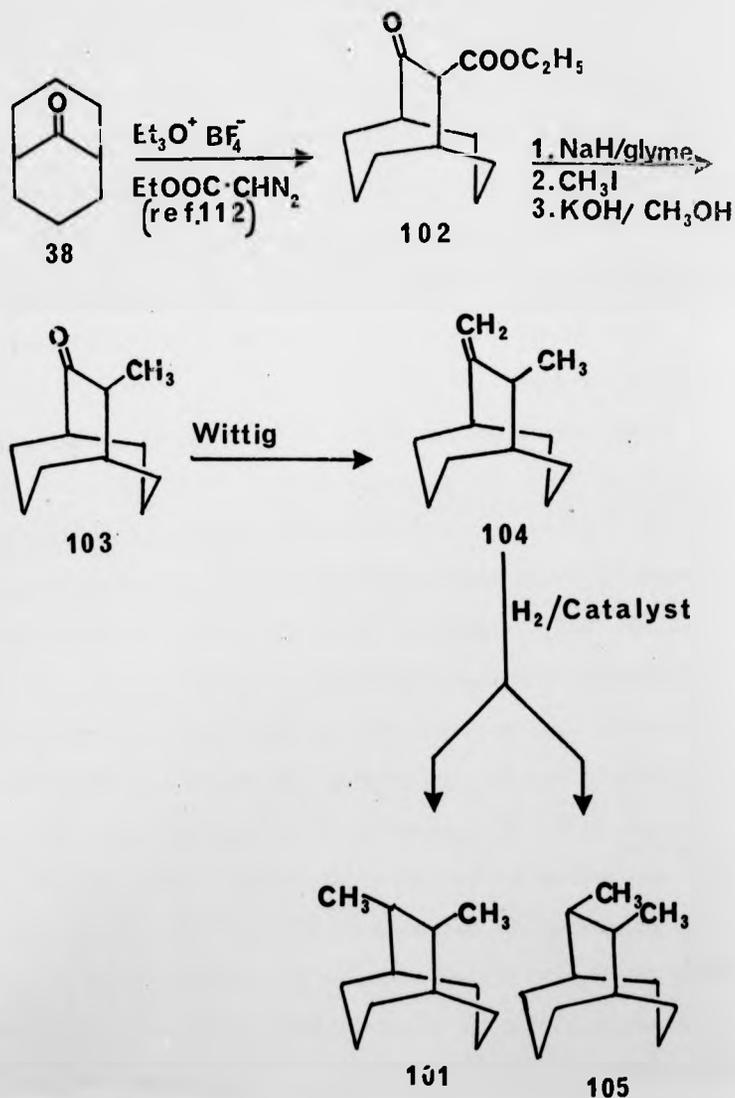
evidence does not prove that this is the only conformation present.

The possibility of a conformational mixture existing in solution for 9-bicyclo(3.3.2)decene (70) has already been mentioned, and taken together with Schleyer's calculated result that the boat-chair and twin-chair conformations are of comparable energy, the possibility of a conformational mixture existing in solution for other bicyclo(3.3.2)decane derivatives cannot be ruled out. In fact, there is evidence from the infra-red spectra that this may indeed be the case.

If we look at the extinction coefficients of the bands at 2980 and 1485 cm.⁻¹ for the compounds in table 3a we find the following decrease in intensity: 9-bicyclo(3.3.2)decanol (24) > bicyclo(3.3.2)decane (1) > 9-bicyclo(3.3.2)decanone (75) > bicyclo(3.3.2)decane-9,10-dione (74) > 9-bicyclo(3.3.2)decene (70). The extinction coefficient of bridgehead substituted compounds such as the bridgehead alcohol (14) is of the same order as that of bicyclo(3.3.2)decane itself, and the frequency of the abnormal bands is constant within the bounds of experimental error (see tables 3a and 3b). It is at once apparent that the band intensity is dependant on the steric requirement of the two carbon bridge - the greater its steric requirement the more intense the abnormal bands.

Since, according to Winstein, differences in the interhydrogen distance affect only the frequency of the bands, but not the intensity,⁷⁴ (which is largely governed by the strength of the coupling), this

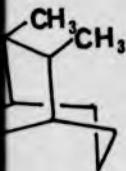
Scheme 1



observed intensity of
 apart of the rings is
 facilitated by the de
 bridge. Thus, the mo
 requirement of the tw
 of boat-chair conform
 decreases. If this
 determining the prop
 present in solution,
 compound in which on
 a compound would be
 as the steric require
 the molecules into th
 outlined in Scheme 1.
 has been prepared by
 sodium hydride in gly
 decarboxylation with
 methyl-9-bicyclo(3.3.
 ketone, as described
 bicyclo(3.3.2)decane
 mixture of *cis*- and
 and 101), which shou
 However, it is quite
 a stereo-specific red

H/glyme →
131
OH/ CH₃OH

catalyst



105

observed intensity difference cannot be due to increased splaying apart of the rings in a twin chair conformation which would be facilitated by the decreased steric requirement of the two carbon bridge. Thus, the most likely explanation is that as the steric requirement of the two carbon bridge decreases, the proportion of boat-chair conformer increases and so the abnormal band intensity decreases. If this is the case, we have a potential method for determining the proportion of twin-chair and boat-chair conformers present in solution, given that we can obtain a spectrum of a compound in which only the twin-chair conformer is present. Such a compound would be trans-9,10-dimethylbicyclo(3.3.2)decane (101), as the steric requirement of the two methyl groups would force all the molecules into the twin-chair conformation. The synthesis is outlined in Scheme 1. 10-Carboxy-9-bicyclo(3.3.2)decanone (102)¹¹² has been prepared by Watt. Methylation of this β -keto-ester with sodium hydride in glyme, and methyl iodide; followed by hydrolysis/ decarboxylation with methanolic potassium hydroxide will give 10-methyl-9-bicyclo(3.3.2)decanone (103). A Wittig reaction on this ketone, as described by Leonard⁴⁵ will give 9-methylene-10-methyl bicyclo(3.3.2)decane (104). Catalytic reduction will yield a mixture of cis- and trans-9,10-dimethylbicyclo(3.3.2)decane (105 and 101), which should be separable by preparative gas chromatography. However, it is quite possible that by suitable choice of catalyst, a stereo-specific reduction to the trans isomer (101) only may well

be effected. Measurements of the extinction coefficient of the 1485 cm^{-1} band of trans-9,10-dimethyl bicyclo(3.3.2)decane (101) and comparison with the extinction coefficients of the compounds in table 3a should give the proportion of the different conformers present, and thus demonstrate the energy difference between the two conformers of bicyclo(3.3.2)decane itself.

In this context, it is worthy of note that the abnormal $\delta(\text{C-H})$ bands observed for bicyclo(3.3.2)decane derivatives are all considerably weaker than those observed by Martin in the bicyclo(3.3.1)nonane series. The extinction coefficients of the band at 1490 cm^{-1} in the spectrum of the 1,5-dimethyl bicyclo(3.3.1)nonane derivatives are recorded in table 1 (above). Since there is no conformational mixture present in solutions of these compounds one might be tempted to use the value of the extinction coefficients in table 1 as a basis for the calculation outlined above. However, one has no way of knowing if the bands are directly comparable in this way, as the bands in the bicyclo(3.3.2)decane compounds may be inherently weaker.

However, if the variation in intensity in the bicyclo(3.3.2)decane series is due to conformational mixtures, one asks why the extinction coefficient of the 1490 cm^{-1} band for 1,5-dimethyl bicyclo(3.3.1)nonane (53) is so much lower than the others, which are remarkably constant. The discrepancy may be due to an error; certainly the absolute accuracy of the extinction coefficients in

table 3a is not high, not least because of the extreme weakness of some of the bands. In the bicyclo(3.3.1)nonane series, though, the bands are both stronger and more completely resolved, which should result in more accurate extinction coefficient measurement.

While trans-9,10-dimethylbicyclo(3.3.2)decane (101) is probably the most suitable compound for determining the true intensity of the abnormal δ (C-H) band for the twin-chair conformation of bicyclo(3.3.2)decane, the steric requirement of trans-9,10-dibromobicyclo(3.3.2)decane (106) is likely to be almost as great. Accordingly, its preparation by addition of bromine to 9-bicyclo(3.3.2)decene (70) was attempted. However, the desired compound could not be obtained by addition of a 0.1M solution of bromine to a solution of the olefin, using either carbon tetrachloride or glacial acetic acid as solvents. Considerably more than the stoichiometric quantity of bromine was absorbed by the olefin, and fumes, presumably of hydrogen bromide were observed. Clearly radical attack on the ring was occurring as well as addition to the double bond. The most likely site for this attack is at the bridgeheads, which even in bicyclo(3.3.2)decane are very reactive (see chapter 2, section ii). In 9-bicyclo(3.3.2)decene the bridgeheads are also in an allylic position, and are therefore likely to be even more reactive. It is noteworthy that Henry found radical attack by bromine at positions 3 and 6 in the homoadamantane ring (positions equivalent to the bridgeheads in bicyclo(3.3.2)decane) to

occur concurrently with Hunsdiecker decarboxylation of homo-¹¹³adamantane-1,8-dicarboxylic acid (107). As a result, attempts to prepare trans-9,10-dibromobicyclo(3.3.2)decane (106) were abandoned. Trans-bicyclo(3.3.2)decane-9,10-diol (108) would also be an interesting compound; certainly it would be expected to have a stronger 1485 cm.^{-1} band than 9-bicyclo(3.3.2)decanol (24). However, the steric requirement of a hydroxyl group is considerably less than that of a methyl group,⁷⁰ and so the extinction coefficient of the 1485 cm.^{-1} band could not be accepted as a basis for the calculation of the ratio of different conformers in solutions of other bicyclo(3.3.2)decane derivatives. Also, molecular models indicate that a strong intramolecular hydrogen bond can be formed if the degree of stagger in the two carbon bridge is large. Such a hydrogen bond could have a profound effect on the conformation of the molecule, and thus render any conformational conclusion incapable of extension to other molecules in the system.

Further, the synthesis of this compound might also prove difficult. Trans-diols are normally prepared by acid cleavage of an epoxide. However, the treatment of 9,10-epoxybicyclo(3.3.2)decane (109) with acid reagents would generate a carbonium ion at position 9, and as well as reacting to give the desired diol (108), this carbonium ion might well undergo either hydride shift or skeletal rearrangement or both. As a result, this synthesis was not attempted.

However, one compound with a large steric requirement on the two carbon bridge was prepared early on in this study, albeit in a crude state. This was 9,10-bis(trimethylsilyloxy)-9-bicyclo(3.3.2)decene (37), prepared by the acyloin condensation of diethyl cyclo-octane-1,5-dicarboxylate (36) in the presence of trimethylsilyl chloride. Strong bands were observed in the infra-red spectrum of a crude sample at 2990 and 1489 cm^{-1} . It was considered that in this case, the bulky trimethylsilyloxy groups would prevent the ring adopting the preferred boat-chair conformation (due to the double bond at position 9) and so the molecule is forced to revert to a twin-chair. The observed frequencies of the abnormal bands are higher than those for other bicyclo(3.3.2)decane derivatives - this is not surprising as the double bond reduces the ability of the ring to flex apart (see above) and so the endo-3- and endo-7- hydrogens are closer than normal. The fact that such bulky substituents can force a 9-bicyclo(3.3.2)decene ring out of the preferred boat-chair conformation shows that suitably bulky substituents on a bicyclo(3.3.2)decane ring will adequately prevent the molecule going into a boat-chair conformation. It is also possible that the bis-trimethylsilyl ether (37) is in fact in a twin-twist-boat conformation, with the abnormal bands arising from a 2,6-transannular interaction. Even if this is the case, however, it does not reduce the validity of the foregoing argument.

Having shown that the steric requirement of the two carbon

bridge appears to control to a large extent the proportion of twin-chair and boat-chair conformers present in solution, we are led to consider that exo-3-bicyclo(3.3.2)decanol (3), of which the NMR spectrum was the original evidence for the twin-chair conformation, will probably exist as a conformational mixture too; if so, this might be detected by low temperature NMR. The C3 carbonyl proton in a boat-chair conformation (cycloheptanol in chair (110)) would not be transannularly deshielded, and so this proton should resonate at about δ 6.2 τ . It is possible that at very low temperatures, the conformational equilibrium might be sufficiently slowed to enable observation of signals due to the boat-chair conformer (110). In this case, it would be possible to determine the conformational free energy for the change from twin-chair to boat-chair, and to see how it varied with temperature.

So far, there is only one piece of quantitative evidence for a similarity of energy for the twin-chair and boat-chair conformations. Dissolving metal reductions of ketones are known to give the more stable isomer, where more than one alcohol is theoretically possible. Thus, the reduction of 3-bicyclo(3.3.1)nonanone (111) with sodium in moist ether gives only exo-3-bicyclo(3.3.1)nonanol (29). This is to be expected, since the twin-chair conformation is more stable than the boat-chair conformation that would be required by endo-3-bicyclo(3.3.1)nonanol (112). However, similar reduction of 3-bicyclo(3.3.2)decanone (32) gives exo- and endo-3-bicyclo(3.3.2)decanols (3 and 4) in the ratio 48:52.

It is suggested that the near equivalence of these figures reflects the almost identical energy content of the twin-chair and boat-chair conformations, at least with an equatorial (or boat-equatorial) 3-hydroxyl substituent. This indicates that Schleyer's calculations may well be largely correct in predicting by and large similar energies for the twin-chair and boat-chair conformations.

We have accumulated evidence which strongly indicates that for compounds in which the two carbon bridge is unsubstituted, the twin-chair, if not the sole conformation present in solution, is at least a major one; while for 9-bicyclo(3.3.2)decene (70) and related compounds in which C1, C7, C10 and C5 are all held coplanar, the boat-chair conformation is preferred. The best way of confirming these theories was an X-ray crystallographic study of suitable compounds.

9-Bicyclo(3.3.2)decene (70) did not promise to be a suitable compound, because of its volatility and its instability in air; further, it does not crystallise satisfactorily. However, 7,8,9,10-tetrahydro-6,10-propano-6H-cyclohepta (b) quinoxaline (76), in which the two carbon bridge of the bicyclo(3.3.2)decane ring forms part of an aromatic system, promised to be an excellent substitute.

The X-ray analysis was carried out in these laboratories by Dr. P. and Dr. J. Murray-Rust. Data were collected on a Hilger-Watts linear diffractometer and the structure was solved by direct methods.

Fig 6

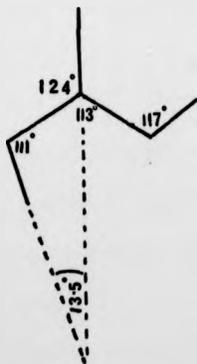
CRYSTAL DATA

$C_{16}H_{18}N_2$ space group $P2_12_12_1$.

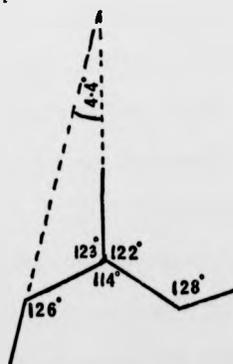
$Z = 4$; $a = 710(1)$; $b = 722(1)$; $c = 2561(2)$ pm. ;

$D_m = 1.23$; $D_c = 1.22 \text{ g.cm}^{-3}$ $R = 8.6\%$.

Angles between molecular planes.

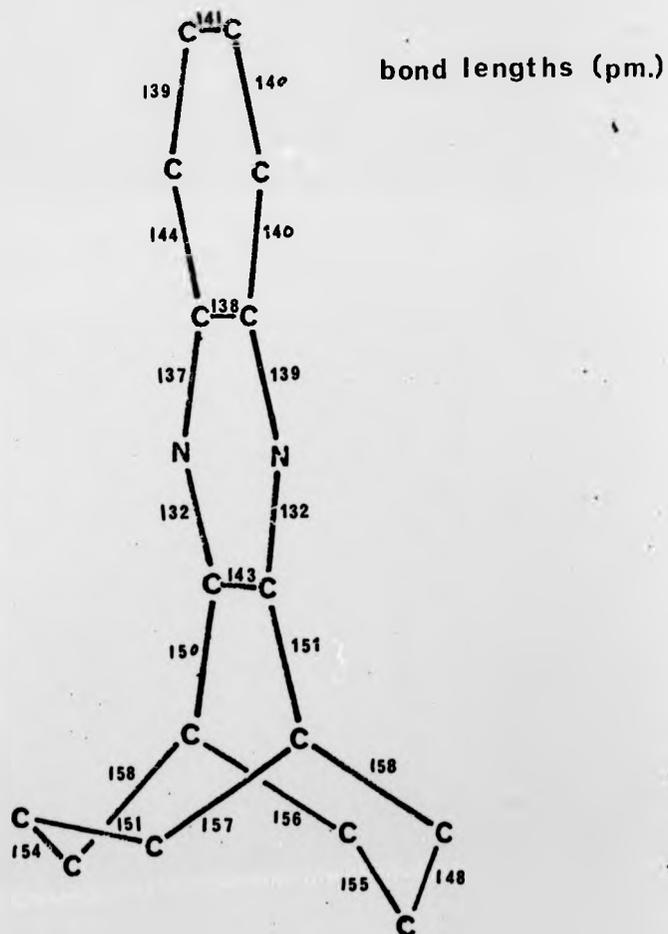


Predicted by
Dreiding model.



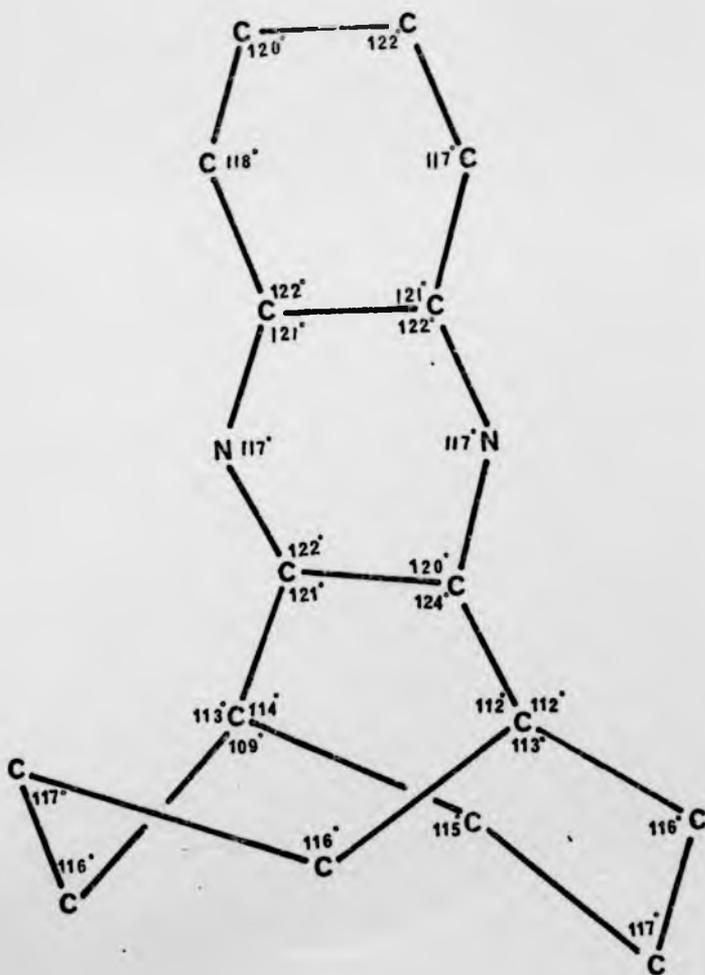
Observed in this
study.

Fig 6a



e.s.d. = 1 pm.

Fig 6b



The crystal data, the
together with a diagram
as compared with the s
predicted boat-chair c
The bond lengths are s
in the aromatic moiety
the plane of the arom
mirror symmetry perpe
actions present in a
between the hydrogens
transannular interact
hydrogens on C7 and C
the eight membered ri
ring bond angles.

Our theory regard
confirmed by this X-r
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Further, bicyclo(3.3.
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The first compound to

The crystal data, the bond lengths and bond angles are in Fig. 6., together with a diagram indicating the degree of ring flattening as compared with the shape predicted by a Dreiding model. The predicted boat-chair conformation was established for this compound. The bond lengths are all within the expected limits and the angles in the aromatic moiety are normal. The bridgehead atoms lie in the plane of the aromatic system, giving the molecule almost complete mirror symmetry perpendicular to this plane. The several interactions present in a Dreiding model (i.e. 1,3-diaxial interactions between the hydrogens on C7 and C9, and between C12 and C14; and a transannular interaction between the endo-hydrogen on C13 and the hydrogens on C7 and C9 are relieved by a considerable flattening of the eight membered ring, and there is a consequent increase in the ring bond angles.

Our theory regarding the boat-chair conformation having been confirmed by this X-ray analysis, we then turned to a suitable compound which was predicted to be a twin-chair. It was essential that the chosen compound should exhibit anomalous δ (C-H) bands in the infra-red both in the solid phase and in solution, as was done in the case of the X-rayed bicyclo(3.3.1)nonane derivative (65). Further, bicyclo(3.3.2)decane itself was unsuitable for the same reasons that ruled out 9-bicyclo(3.3.2)decene. Since any substitution other than at the bridgeheads would affect the structure in some way or other, only bridgehead substituted compounds could be considered. The first compound to be examined was 1-bicyclo(3.3.2)decanol (14),



but this was found to have a disordered crystal structure. Attention then turned to bicyclo(3.3.2)decane-1,5-diol (39) which at first was more promising, but proved to be very difficult to solve by direct methods, being a tetragonal structure. As a result, 1,5-dichlorobicyclo(3.3.2)decane (78) was synthesised, and Dr. P. Murray-Rust is currently examining this compound, while continuing to also examine the bridgehead diol.

Both these compounds display abnormal scissoring bands in both solid and solution spectra, and therefore both are predicted to adopt a twin-chair conformation in a crystal, and be mainly in the twin-chair conformation in solution.

One other conformational probe that was thought early on should give useful information regarding the preferred conformation of bicyclo(3.3.2)decane was ^{13}C NMR. Fourier transform ^{13}C NMR spectra were recorded for bicyclo(3.3.2)decane (1), 9-bicyclo(3.3.2)decanone (75), bicyclo(3.3.2)decane-9,10-dione (24) and 9-bicyclo(3.3.2)decene (70). Unfortunately, no conformational information could be obtained from these spectra. It was hoped, in particular, that the chemical shift of C3 in the boat-chair conformation of 9-bicyclo(3.3.2)decene (70) would be significantly different from the chemical shift in twin-chair conformations of the other compounds. With the evidence of considerable ring flattening in the boat-chair conformation, from the X-ray study of the quinoxaline (76), however, one is not so surprised to find that in fact there is no significant

chemical shift difference as C3 will be well separated from the shielding zone of the double bond in the 9-bicyclo(3.3.2)decene.

We now turn to the question of whether the two-carbon bridge is staggered or eclipsed. We have already seen that there is a considerable body of evidence for an eclipsed bridge in homoadamantane derivatives, which are structurally very closely related to bicyclo(3.3.2)decane derivatives. The conformational probes used in the homoadamantane series have proved fruitful in the bicyclo(3.3.2)decane series also.

35
Thus, Doyle³⁵ noted that the carbonyl stretching frequency of 9-bicyclo(3.3.2)decanone (75), *viz.* 1697 cm.^{-1} , constitutes evidence for an eclipsed bridge in this derivative. This carbonyl stretching frequency corresponds to a $\text{C}-\overset{\ominus}{\text{C}}-\text{C}$ bond angle of about 127° (for a fuller discussion of how this value is reached, see Chapter 2, section iii). Such a bond angle is found in molecular models of a conformation with an eclipsed bridge; if the bridge were in fact staggered, a normal bond angle of 120° (corresponding to a carbonyl stretching frequency of 1720 cm.^{-1}) would be easily accommodated. Further, Doyle also reports that the bridge (C10) protons in this compound (75) are observed in the NMR as a sharp doublet, $J_{AX} = 6\text{ Hz}$. This shows that the protons on C10 are equivalent, and thus the two carbon bridge is either eclipsed or in rapid equilibrium. No variable temperature studies have been carried out on this compound.

The visible spectrum of bicyclo(3.3.2)decan-9,10-dione (74) was also expected to shed light on the question of the dihedral

114
angle of the two carbon bridge. Leonard and Mader have determined the ultra-violet and visible spectra of a series of non-enolisable α -diketones; they showed that the position of the band in the longer wavelength visible region is qualitatively dependant on the dihedral angle between the two carbonyl groups. As noted earlier, Schlattmann⁶⁵ interpreted the λ_{\max} of 418 nm for homoadamantane-4,5-dione (50) (shown by X-ray⁶⁴ to correspond to a dihedral angle of 11.9°) as evidence for an essentially eclipsed bridge in homoadamantane itself. For bicyclo(3.3.2)decan-9,10-dione (74), λ_{\max} was found to be 421 nm. The closeness of this figure to that observed for the homoadamantane derivatives (50) suggests that the dihedral angle in bicyclo(3.3.2)decan-9,10-dione is only marginally greater than that for homoadamantan-4,5-dione. This would suggest an angle no greater than 12.5° , which is considerably less than the 22° quoted by Schleyer as the dihedral angle giving the lowest energy for the twin-chair conformation of bicyclo(3.3.2)decane, and suggests that the dihedral angle in bicyclo(3.3.2)decane itself may well be little greater than 0° . However, the infra-red studies suggest that a very considerable percentage of bicyclo(3.3.2)decan-9,10-dione may well be in a boat-chair conformation, and so the λ_{\max} could well be affected by those molecules in a boat-chair conformation.

Finally, a high resolution NMR study of bicyclo(3.3.2)decane itself has been initiated, but as yet the full results are not to hand. However, the spectrum shows a considerable similarity to that reported for homoadamantane by Schleyer; but in view of the apparent

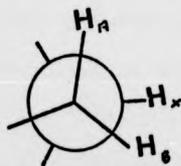
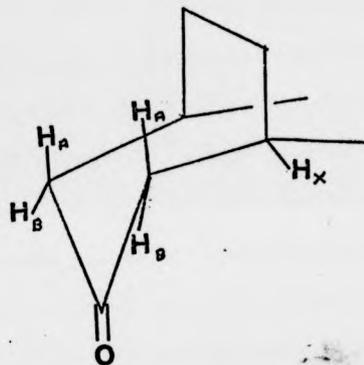
errors in Schleyer's assignments (see above) it is not clear exactly what the significance of this will be, until the decoupling studies at present being carried out are complete.

It is thus clear that there is a considerable body of evidence for an eclipsed two carbon bridge in the bicyclo(3.3.2)⁹⁷decane ring, contrary to earlier ideas. It is difficult to tell, though, whether this is a fixed conformation, or the result of rapid equilibration through a mean eclipsed position. Since Schleyer has predicted the presence of broad energy wells in the conformation of homodamantane, and in the boat-chair and twin-boat conformations of bicyclo(3.3.2)decane (though not the twin-chair conformation), such an equilibrium may well not be detectable by low temperature NMR, and definite proof one way or another might prove very difficult.

Before closing this chapter, it is interesting to consider what other evidence there is for conformations of other derivatives of bicyclo(3.3.2)decane.

3-Bicyclo(3.3.2)decanone (82) is particularly interesting in that the insertion of a trigonal sp^2 centre at C3 removes many of the interactions present in bicyclo(3.3.2)decane itself. The high resolution (220 MHz.) NMR spectrum of this compound is most informative. The protons α to the carbonyl group are coupled only to the bridgehead protons, and form the AB part of an ABX (or

Fig 7



rather 2 equivalent AB
quartet, with subsidiary
head proton). $J_{AB} = 1$
equal to J_{AX} and J_{BX} at
axial α -hydrogen and B
couplings of the magni
for if the carbonyl gr
with the bridgehead pr
the two α -methylene pr
was in a ring in a bo
would be eclipsed by t
nearly perpendicular t
would be manifest by J
boat axial proton and

Further, from the
it is possible to com
orientation of the ca
protons. Schmid et.
constants of a large
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116
Grant have analysed
of an adjacent π -bond
both a theoretical an
 π -contribution to the
0 to -4 Hz., the exact

rather 2 equivalent ABX) systems. The protons appear as an AB quartet, with subsidiary splittings due to the X-proton (bridgehead proton). $J_{AB} = 17$ Hz., and the minor splittings, approximately equal to J_{AX} and J_{BX} are $J_{AX} = 3$ Hz. and $J_{BX} = 5$ Hz. where A is the axial α -hydrogen and B is the equatorial α -hydrogen. Vicinal couplings of the magnitude of 3 Hz. and 5 Hz. can only be accounted for if the carbonyl group is in a ring in a chair conformation, with the bridgehead proton X almost bisecting the angle between the two α -methylene protons (see fig. 7). If the carbonyl group was in a ring in a boat-conformation, one of the α -methylene protons would be eclipsed by the bridgehead proton, and the other would be nearly perpendicular to the bridgehead proton. Such a situation would be manifest by $J_{AX} = 10$ Hz. and $J_{B'X} = 0$ Hz., where A' is the boat axial proton and B' the boat equatorial proton.

Further, from the very large geminal coupling, $J_{AB} = 17$ Hz. it is possible to come to some conclusion about the relative orientation of the carbonyl group relative to the α -methylene protons. Schmid et. al.¹¹⁵ have determined the geminal coupling constants of a large number of substituted cycloheptanes, and found a fairly constant figure of -13.5 to -14 Hz. Barfield and Grant¹¹⁶ have analysed the effect on the geminal coupling constant of an adjacent π -bonded system, including carbonyl groups, using both a theoretical and an experimental approach; they find a π -contribution to the geminal coupling constant which varies from 0 to -4 Hz., the exact value depending on the dihedral angle between

the methylene group and the adjacent π -bond. Thus, for 3-bicyclo(3.3.2)decanone, there appears to be a π -contribution of -3 to -3.5 Hz., assuming that the geminal coupling constant is negative. The dihedral angle predicted by a Dreiding model is 75-80°, which corresponds to a π -contribution of approximately zero, while the dihedral angle calculated from the observed π -contribution is between 45° and 50°. This means that the cycloheptanone ring in the already proven chair conformation must be splayed outwards by about 30°, resulting in considerable angle strain, which is itself manifest in the carbonyl stretching frequency of 1692 cm^{-1} for 3-bicyclo(3.3.2)decanone (equivalent to a $\widehat{\text{C}}-\text{CO}-\text{C}$ bond angle of 132.5°).

While it is not possible to determine the rest of the conformation of 3-bicyclo(3.3.2)decanone directly from the NMR spectrum, it is probable that with the aid of spin decoupling studies, such a determination might well be achieved.

Chapter 2

The Reactivity of the Bicyclo(2.3.2)decane System

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Section (i)

Transannular Hydride Shifts in the
Bicyclo(2.3.2)decane System

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Transannular Hydride Shifts in the Bicyclo(3.3.2)decane System

Now that we have built up a satisfactory conformational picture of the bicyclo(3.3.2)decane system, we are ready to examine the reactivity of various derivatives of bicyclo(3.3.2)decane. The greater part of the reactivity studies carried out to date on this system are concerned with the problems of transannular hydride shifts.

In 1944 the classic and elegant experiments of Bartlett et. al.¹¹⁷ showed that hydride transfer from a non-activated CH₂ group to a carbonium ion can occur with great rapidity, but with the exception of special situations, such as 1,2-hydride shifts and cases where the product of reaction with solvent regenerates the carbonium ion,¹¹⁸ hydride shift was not found to compete successfully with solvent capture by the initially formed carbonium ion.

However, Prelog¹¹⁹ and Cope⁹ both discovered in 1952 that a transannular hydride shift can compete effectively with a nucleophilic solvent for the carbonium ions of medium rings. Since then, much work has been carried out, by Prelog¹⁴ and by Cope and by others,⁸ but the relative importance of such factors as proximity of the CH₂ group to the cation, ring strain, and hindrance to reaction with solvent is not yet clear, nor is it known whether the mechanism is stepwise, or fully or partially concerted. Other factors almost certainly influencing hydride shifts are the magnitude of conformational barriers, the nucleophilicity and acidity of the reagent, the molecular size of the reagent and the reaction temperature.

Fig 1a

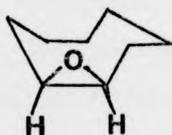
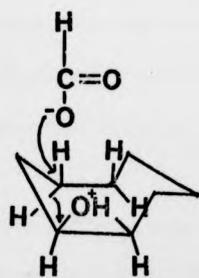
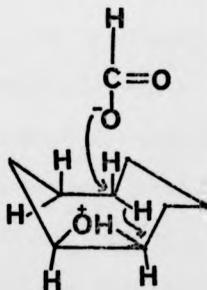


Fig 1b



1,3-hydride
shift

Fig 1c



1,5-hydride
shift

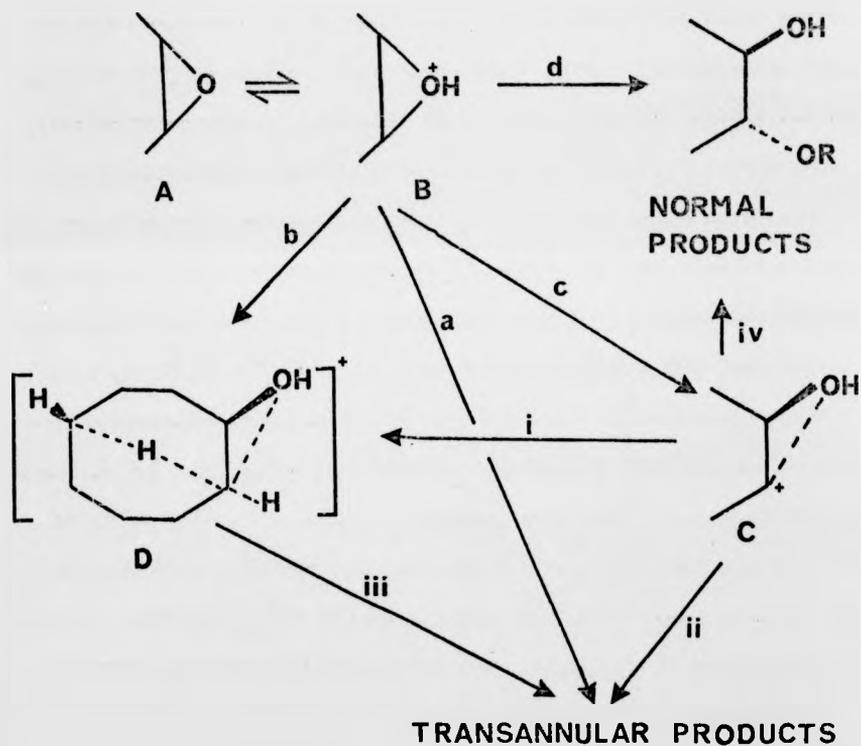
Cope's first observation⁹ of cis-cyclo-octane oxide (113). It was found that con-
cis-cyclo-octane-1,4-
 expected trans-cyclo-
 products viz. 3- and
 with several minor pro-
 products arose from a
 cyclo-octene oxide (114).
 showed that 61% of cis-
 1,5-hydride shift and
 the 3-cyclo-octanol (115)
 to result from a 1,5-h-

A recent NMR study¹²³ has demonstrated that¹²⁴ the
 by Hendrickson (Fig. 1c) understanding these re-
 Fig. 1c) must involve
 while the less favoured
 involves transfer from
 of cis-cyclo-octene ox-
 axial hydrogen on C5 to
 C4 approach to C2.

Cope's first observations were of the formolysis of cis-cyclo-octene oxide (113). After hydrolysis of the intermediate formates, it was found that considerable quantities of transannularly derived cis-cyclo-octane-1,4-diol (114) were formed^{10,11} in addition to the expected trans-cyclo-octane-1,2-diol (115). Transannular elimination products viz. 3- and 4-cyclo-octenols (116 & 117) were also formed^{120,121} with several minor products. To determine whether the transannular products arose from a 1,3- or a 1,5-hydride shift, 5,6-dideutero-cis-cyclo-octene oxide (118) was formolysed;¹²² degradation of the product showed that 61% of cis-cyclo-octane-1,4-diol (114) was formed by a 1,5-hydride shift and the remaining 39% by a 1,3-hydride shift. For the 3-cyclo-octenol (116) formed in the same experiment, 94% was found to result from a 1,5-hydride shift.

A recent NMR study of 1,3,3-trideutero-cyclo-octene oxide (119)¹²³ has demonstrated that this compound adopts the conformation suggested by Hendrickson¹²⁴ (Fig. 1a). This conformation provides a basis for understanding these results. The preferred pathway (1,5-hydride shift, Fig. 1c) must involve transfer of the axial hydrogen on C5 to C1, while the less favoured route (1,3-hydride shift, Fig. 1b) presumably involves transfer from C4 to C2. An examination of a molecular model of cis-cyclo-octene oxide in the preferred conformation shows that the axial hydrogen on C5 can approach closer to C1 than can a hydrogen on C4 approach to C2.

Scheme 1

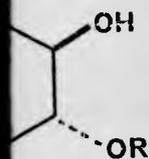


after Cope¹²

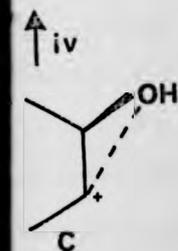
Cope has also
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Cope has also studied the solvolysis of cis-cyclo-octene oxide¹² with various acids and shown that the extent to which transannular reactions occur depends on acid strength. Trifluoroacetic acid gave only transannular products, while buffered acetic acid gave only 24% of compounds formed by transannular pathways. Trichloroacetic acid, formic acid and unbuffered acetic acid all gave varying mixtures of transannular and normal products lying between these two extremes, with the stronger acids giving rise to more transannular products. Pimelic acid was not strong enough to give any reaction, even at 170°.

Whereas there was a good correlation between acid strength (expressed as the dissociation constant in water) and the extent of transannular reaction, there was no obvious correlation with either the size of the nucleophile or the dielectric constant of the reaction medium. The effect of acid strength is understandable, since in a less nucleophilic medium, the nucleophilic contribution of the migrating hydride becomes more significant than it is in a more nucleophilic medium.

¹²
Cope then developed a reaction scheme for epoxide solvolysis¹³ (Scheme 1). Because of Prelog and Borcic's observation of no deuterium isotope effect in the solvolysis of 5,5,6,6-tetradeuterocyclohexyl tosylate, which does involve a transannular hydride shift,¹²⁵ (the validity of this result has since been questioned by Borcic,¹²⁶ because of the ambiguous method of introducing the deuterium label) Cope

interpreted his results in terms of path c, involving rate determining formation of a classical carbonium ion C in which some tetrahedral configuration is maintained. (This is necessary to account for the stereo-specificity of the subsequent reaction steps). Transannular reaction from carbonium ion C may either go by an intermediate bridged carbonium ion D by path I followed by path III; or directly by path II. Normal products are formed by path IV, or directly by an S_N2 mechanism, from the initial protonated epoxide B.

In this mechanistic scheme, it is clear that there is competition between paths (i) and/or (ii), and path (iv), in which the nucleophilicities of the solvent and the migrating hydride are the factors governing the ratio of transannular to normal reaction.

127
Cope has also performed a very elegant study of the solvolysis of 1,2,2,8,8-pentadeuterocyclo-octyl tosylate (120). Trifluoroacetic acid, formic acid and buffered acetic acid solvolyses were carried out and subsequent degradation of the cis-cyclo-octene and the cyclo-octanol derived from the acid esters, followed by careful mass spectral analysis of the deuterium content, showed that the extent of 1,5-transannular hydride shift was 62%, 60%, and 53% respectively.

128
Roberts and Anderson have solvolysed a series of deuterated cyclo-octyl tosylates; as well as carrying out conventional kinetic studies, the solvolyses were also followed by 100 MHz. NMR. Solvolysis of 1-deuterocyclo-octyl tosylate (121) showed after 1 half-life, a

signal corresponding to the carbinyl proton in cyclo-octyl tosylate, amounting to 20% of the unreacted tosylate. This was considered evidence for return from ion pair intermediates which had undergone 1,5-hydride shift. Since there was no observed special salt effect with lithium perchlorate, and since the return to rearranged tosylate was not affected by the added salt, Roberts and Anderson concluded that hydride shift could take place in an intimate ion pair, and thus that hydride shift can occur before the rate determining step.

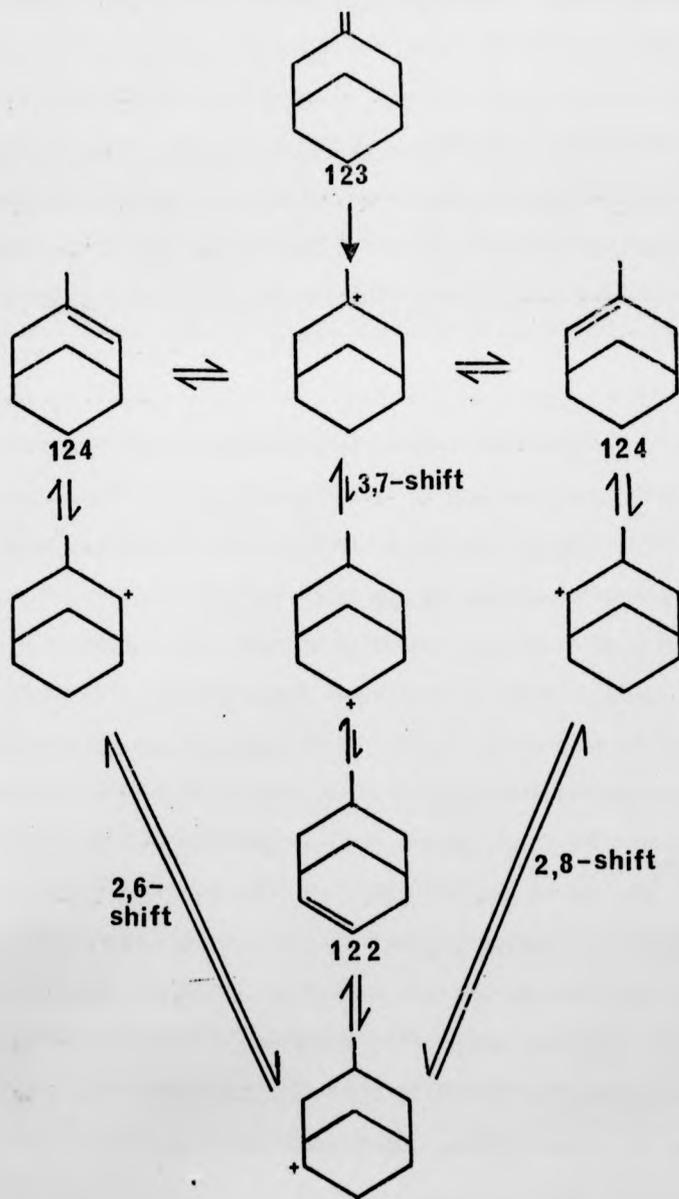
From their kinetic data, Roberts and Anderson concluded that the deuterium isotope effect ($k_H/k_D = 1.02$ per deuterium atom) was probably a secondary isotope effect; and could be due solely to a remote secondary isotope effect without hydride participation, perhaps caused by a decrease in ground state strain as suggested by Prelog as explanation for the 1.02 isotope effect found in 5,5,6,6-tetradeutero decyl tosylate solvolysis. (But see also comment above and ref. 126).¹³ However, they also considered the possibility of its being a primary isotope effect associated with participation. In this case, the fraction of hydride assisted ionisation is calculated to be about $\frac{1}{4}$; that is, most of the hydride shift occurs after rate determining ionisation.

As well as examining the transannular reactions of cis-cyclo-octene oxide in acidic media, Cope has also discovered transannular reactions during acid solvolysis of cycloheptene oxide and trans-¹²⁹

cyclo-octene oxide,¹³⁰ though only to the extent of 2.4% in the former case. Prelog has observed transannular reactions during hydroxylation with performic acid of cyclononene,¹³¹ cyclodecene,¹¹⁹ and cycloundecene.¹³² However, transannular reactions are not confined to acid catalysed reactions. Gono has treated cis-cyclo-octene oxide with lithium diethylamide, a strong, non-nucleophilic base; in this case the transannular product (70%) was the ring closed endo, cis-2-bicyclo(3.3.0)octanol; the normal product was 2-cyclo-octanol (16%).¹³³

One of the problems inherent in the study of these systems is the conformational mobility of the ring systems; indeed, as noted earlier it is only at the time of writing that reliable information regarding the conformation of cis-cyclo-octene oxide has come to hand. As a result, study turned instead to bridged ring systems in which the conformational mobility of the medium ring carbonium ions is restricted, and bicyclo(3.3.1)nonane rapidly became a popular system in which to study transannular reactions, once the twin-chair conformation had been established. The first hydride shift in this system was reported by Graham,¹³⁴ who showed that both exo-7-methylbicyclo(3.3.1)non-2-ene (122) and 3-exomethylene bicyclo(3.3.1)nonane (123) were converted by boiling formic acid to the same mixture of 3-methylbicyclo(3.3.1)non-2-ene (124) (93%) and exo-7-methylbicyclo(3.3.1)non-2-ene (122) (7%). The results were interpreted in terms of a 3,7-hydride shift, but there was no proof of this, and it could be a 2,6-hydride shift

Scheme 2

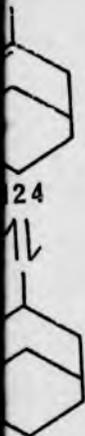


or a combination of
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 Thus exo-3-hydroxy-
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or a combination of the two (see scheme 2). 3,7-hydride shifts have been unambiguously demonstrated in the bicyclo(3.3.1)nonane system. Thus exo-3-hydroxy-endo-3-deutero-7-exomethylene bicyclo(3.3.1)nonane (125) is isomerised in concentrated sulphuric acid to exo-7-methyl-endo-7-deutero-3-bicyclo(3.3.1)nonanone (126)⁴⁹. NMR spectra of starting material and products showed the specific 3,7-hydride shift. Buffered acetolysis of exo-3, exo-7-methylbicyclo(3.3.1)nonyl tosylate (127) gives rise to 55% hydride shift; ⁴⁹ as does solvolysis of the endo-7-deutero analogus (128). In these cases the hydride shift was not rigorously shown to be specifically from C3 to C7, but the specific formation of a C3 carbonium ion and the absence of any products substituted at position 2 together constitute very strong evidence for a specific 3,7-hydride shift.

Kato¹³⁵ has photolysed 4-phenylbicyclo(3.3.1)non-2-ene (129) in the presence of acetic acid, to give a mixture of endo-2-acetoxy-4-phenylbicyclo(3.3.1)nonane (130) and exo-7-acetoxy-4-phenylbicyclo(3.3.1)nonane (131). The former product is considered to arise from addition of acetate to the carbonium ion at C2, which arises from protonation of the photo-intermediate at C3; while the latter is considered to arise from protonation at C2, giving rise to a carbonium ion at C3 which undergoes a 3,7-hydride shift before counter ion capture.

Specific 3,7-transannular ring closure reactions occur during acetolysis of 7-exomethylene-exo-3-bicyclo(3.3.1)nonyl tosylate (132),



shift

giving 1-adamantyl acetate (133),¹³⁶ and during pyrolysis of 3-bicyclo
(3.3.1)nonane tosylhydrazone (134) to give noradamantane (135).¹³⁷

Finally, exo-2,3-epoxybicyclo(3.3.1)nonane (136) has been
solvolysed by Graham¹³⁸ and Marvell,¹⁵ and shown to undergo 3,7-
hydride shifts. Trifluoroacetolysis¹⁵ gave 100% hydride shift and
only products by an elimination pathway; buffered acetolysis¹⁵ gave
about 50% hydride shift in the elimination products and 10% hydride
shift in the products from solvent capture. Interestingly, Graham¹³⁸
has reported a complete absence of hydride shift in the formolysis of
both syn- and anti-9-hydroxy-exo-2,3-epoxybicyclo(3.3.1)nonanes (137
& 138), though hydride shift occurs normally on a formolysis of the
unsubstituted epoxide (136). The sole product for the formolysis of
the syn-hydroxy epoxide (137) is reported to be exo-2-endo-3-syn-9-
bicyclo(3.3.1)nonanetriol (139), and that from formolysis of the anti-
hydroxy epoxide (138) is exo-2-anti-9-bicyclo(3.3.1)non-3-enediol (140).
No explanations of these surprising phenomena have been forthcoming.

Apart from these reactions just mentioned, it is clear that 3,7-
hydride shifts are quite facile processes in the bicyclo(3.3.1)nonane
system. Eakin's observation of only 3.5% hydride shift in the solvolysis
of 7-¹⁴C-exo-3-bicyclo(3.3.1)nonyl tosylate (141),⁴⁸ at least in the
major (95%) product, 2-bicyclo(3.3.1)nonane (27) was therefore both
interesting and surprising.

Since Eakin had found no kinetic isotope effect in the solvolysis
of endo-7-deutero-exo-7-methyl-exo-3-bicyclo(3.3.1)nonyl tosylate (128),⁴⁹

38 35 12
he and Doyle considered, like Cope that hydride transfer took place after the ionisation step. There appeared, therefore, three possible explanations for the low amount of hydride shift in the solvolysis.

a) Since the solvolysis was carried out by sealing the reactants into a tube and raising the reaction temperature to 80°, it was possible that most of the 2-bicyclo(3.3.1)nonene (27) was being formed by a thermal elimination process, since the tosylate in question (141 or 142) was known to be unstable above 30°. However, Barbour¹³⁹ has solvolysed 2,2,3,4,4-pentadeutero-exo-3-bicyclo(3.3.1)nonyl tosylate (143) at 25° and found less than 5% hydride shift in the olefinic fraction.

b) Work by Shiner¹⁴⁰⁻¹⁴² has demonstrated a conformational dependence of β -deuterium isotope effects during the solvolysis of cyclohexyl brosylates that is best explained by a twist-boat conformation in the transition state. These observations have been supported by work by Saunders,¹⁴³ Whiting,^{144,145} and Sicher¹⁴⁵, whose results were also best understood in terms of a twist-boat conformation. Since exo-3-bicyclo(3.3.1)nonyl tosylate (142) is a substituted cyclohexyl tosylate, the distinct possibility exists that this compound might also solvolyse via some type of boat conformation in the transition state, in

which case a 3,7-hydride shift would be greatly inhibited. It is pertinent that the structure of the bicyclo(3.3.1) nonane ring is such as to preclude a twist-boat conformation for one ring while the other is still in a chair conformation. A twin-twist-boat conformation is possible, but this requires two conformational flips, one for each ring. Thus for this explanation to be valid, the tosylate (142) would have to solvolyse either via a very strained extreme-boat-chair conformation (144) or a twin-twist-boat conformation (145).

¹⁴⁶ Curisson and ¹⁴⁷ Stehelin have solvolyzed in aqueous ethanol exo-7,9,9-trimethyl-exo-3-bicyclo(3.3.1)nonyl tosylate (146), in which the reaction must occur in a purely twin-chair transition state, due to the conformational blocking effect of the 9-gem-dimethyl group. They found that hydride shift occurred to the extent of 100% (as compared with 55% ^{49,148} for the lower homologue without the 9-gem-dimethyl group). While this does not constitute proof for the suggestion that exo-3-bicyclo(3.3.1)nonyl tosylate (142) is solvolysing in a boat conformation, whence the small hydride shift, this result does support the idea, and further, it demonstrates a very powerful conformational effect on the degree of hydride shift.

c) It is possible that in a kinetically controlled solvolysis,

the close approach of C3 and C7 in the 3-bicyclo(3.3.1) nonyl cation (41) cannot be realised without incurring prohibitive ring strain, due to the constraint imposed by the C9 bridge. Thus, the preference of the ion to undergo reaction by a normal or a transannular pathway would be determined by the distance between the potentially migrating hydrogen atom and the developing carbonium ion, which distance would be largely governed by the strain in the carbonium ion.

It was in order to test this third hypothesis that Doyle solvolysed 2,2,3,4,4-pentadeutero-~~exo~~-3-bicyclo(3.3.2)⁵⁰ decyl tosylate (147). It was predicted, on account of the much greater flexibility of the bicyclo(3.3.2)decane system (see Chapter 1) that C3 and C7 should be able to approach more closely in a high energy transition state, thus permitting a greater proportion of the intermediate carbonium ion to undergo transannular hydride shift. In the event, it was found that in the major (94%) solvolysis product, 2-bicyclo(3.3.2)decene (20), there was between 42 and 48% hydride shift. This seemed convincing evidence in favour of the strain and flexibility hypothesis, and Ourisson's result¹⁴⁶ on the 7,9,9-trimethyl tosylate (146) could also be interpreted in terms of a distance effect, the 9-~~gem~~-dimethyl group forcing the C3 and C7 termini into greater proximity.

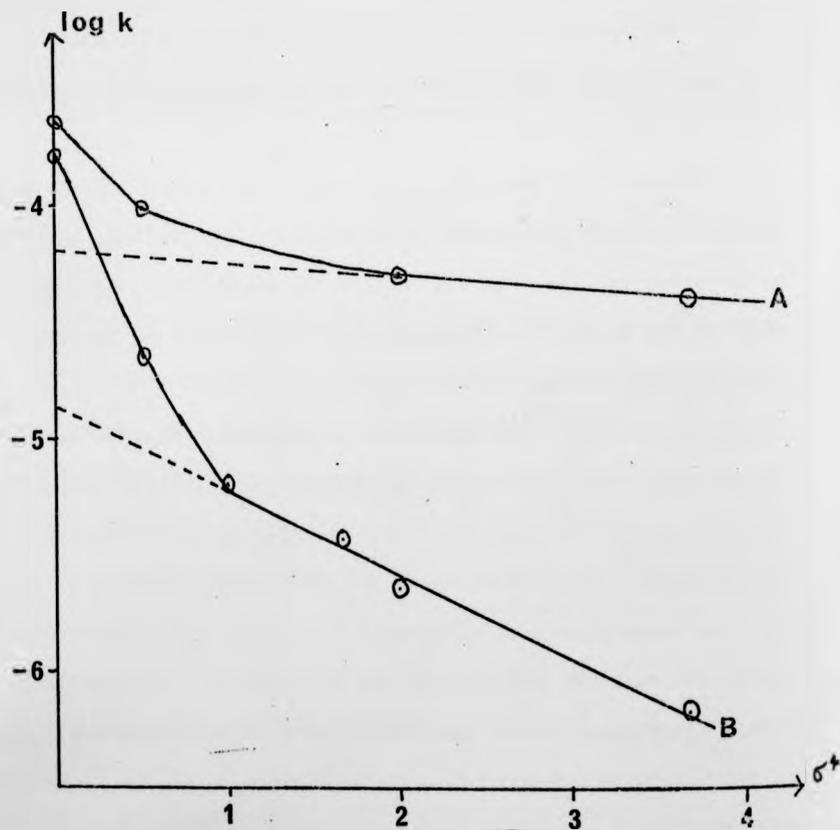
In this context it would be of interest to examine the infra-red spectrum of 9,9-dimethylbicyclo(3.3.1)nonane (148) to see if the abnormal $\nu(\text{C-H})$ and $\delta(\text{C-H})$ bands are at a higher frequency than the 2990 and 1490 cm^{-1} noted for bicyclo(3.3.1)nonane itself; higher frequencies would be indicative of a shorter interhydrogen distance.

However, even more significant is that Curisson has demonstrated migrating hydride participation during solvolysis, in both the bicyclo (3.3.1)nonane¹⁴⁸ and longifolene systems,¹⁴⁹ thus disproving the original assumption behind the foregoing arguments. Nevertheless, participation by migrating hydride does not detract in the slightest from the significance of the much greater hydride shift that occurs in the bicyclo (3.3.2)decane system.

Since Curisson¹⁴⁸ has specifically demonstrated participation during the solvolysis of exo-7-methyl-exo-3-bicyclo(3.3.1)nonyl tosylate (127), in which system participation had previously been specifically ruled out by Eakin,⁴⁹ it is necessary to consider these results more closely.

The techniques used to demonstrate hydride participation in solvolysis were the same in both the longifolene¹⁴⁹ and bicyclo(3.3.1)nonane¹⁴⁸ systems. In the work on the bicyclo(3.3.1)nonanes, a series of exo-7-substituted-exo-3-bicyclo(3.3.1)nonyl tosylates (149) were synthesised and solvolysed in aqueous ethanol. Four compounds were used, the exo-7-substituents being cyano (149, $\text{R}=\text{CN}$), carbomethoxy

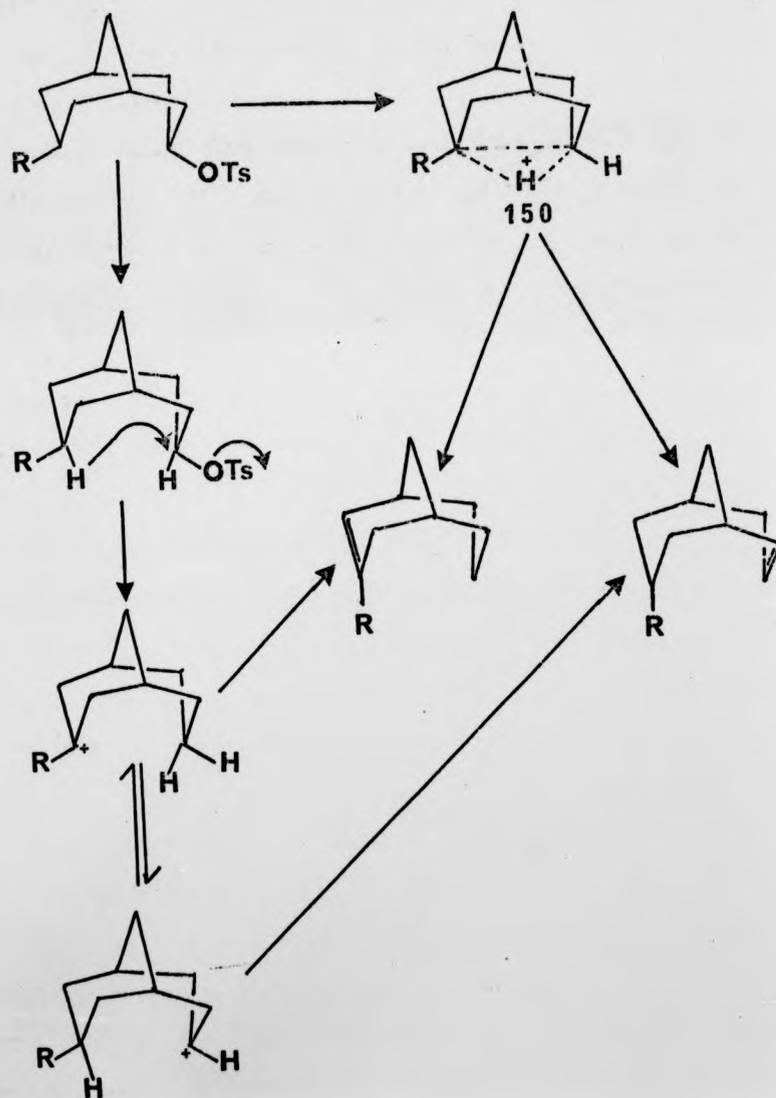
Fig 2



A bicyclo[3.3.1]nonane series¹⁴⁸

B longifolene series¹⁴⁹

Fig 3



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 The kinetic data we
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(149, R=COOCH₃), methoxymethyl (149, R=CH₂OCH₃) and methyl (R=CH₃).

The kinetic data were analysed by a Taft-Hammett plot, $\log k = f(\sigma^*)$ ¹⁵⁰ which was clearly non linear. With the strongly electron attracting groups, cyano and carbomethoxy, no hydride shift was expected; product analysis showed that there was none. With a methoxymethyl substituent there was 10% hydride shift, and with a methyl group there was 5% hydride shift. In these last two cases, the solvolysis rate was augmented beyond that predicted by linear extrapolation of the Taft-Hammett plot for the first two cases (see Fig. 2). A similar, though more pronounced effect was observed for the longifolene case (see Fig. 2).

Since the rate of solvolysis with hydride shift is greater than the calculated solvolysis rate for the same compound in the absence of hydride shift, and since the greater the proportion of hydride shift the greater the rate enhancement, it is clear that there is participation in the rate determining step (presumably the ionisation step) by the migrating hydride.

Unfortunately, Ourisson's studies do not define the structure of the first intermediate in the solvolysis; this could either be a bridged non-classical ion (150) which could collapse one of two ways to yield normal or transannular products, or a transannular ion derived from an intramolecular S_N2 reaction by the migrating hydride, which then equilibrates in a subsequent step to yield the normal ion, hence the product mixture (see Fig. 3).

There is still the discrepancy between Curisson's ¹⁴⁸ and Eakin's ⁴⁹ results to account for. Curisson ¹⁴⁹ does not believe that Eakin's observed absence of a kinetic isotope effect constitutes proof of the absence of hydride participation. ¹⁵¹ Bantorpe has calculated that low isotope effects will occur when the transition state resembles either reactants or products, and that only for intermediate cases will the full theoretical maximum be observed in the solvolytic production of carbonium ions, the transition state is very close to the first reaction ^{152,153} intermediate. Because hydride shift in the solvolysis of exo-7-methyl-exo-3-bicyclo(3.3.1)nonyl tosylate (127) results in conversion of a secondary carbonium ion to a tertiary carbonium ion, the first intermediate, and therefore the transition state is likely to be sufficiently asymmetric as to preclude any kinetic isotope effect. ¹⁵² A further consideration is that Hammond has argued that in a highly exothermic reaction, any isotope effect might be undetectably small because only a slight weakening of the C-D bond would bring the reacting species to the transition state; as an example he cites the work of Lewis ¹⁵⁴ and Boozer who observed no isotope effect in the loss of protons or deuterons from partially deuterated sec-amyl cations. However, since the heat of reaction for the solvolysis of exo-7-methyl-exo-3-bicyclo(3.3.1)nonyl tosylate (127) is not known it is not possible to come to any conclusion about the effect of this factor on any kinetic isotope effect. The important point when dealing with kinetic isotope effects is that the absence of any isotope effect only means that the zero point energies associated with the bending and stretching of the C-H(D) bond in question are not significantly altered in going from reactants to

the transition state.

Using a Foote-Schleyer correlation, Eakin was able to account for the solvolysis rate of exo-3-bicyclo(3.3.1)nonyl tosylate (142) and thus drew the conclusion that there was no anchimeric assistance during the solvolysis. From Ourisson's work it appears that there will be assistance, but as the proportion of hydride shift is small, so the amount of assistance will also be very small. In this system, because it is asymmetrical, the migration being from one secondary centre to another, an appreciable isotope effect might well be expected; but again, the proportion of hydride shift is so small that the isotope effect would also be small. Because of the very minor amount of anchimeric assistance, therefore, it is hardly surprising that Eakin was not able to detect it by application of the Schleyer equation. It is perhaps worthy of note that the Foote-Schleyer treatment would predict similar solvolysis rates for both the exo-7-methyl-3-tosylate (127) and the nor-methyl tosylate (142). In fact the exo-7-methyl-3-tosylate (127) is slightly more reactive towards acetolysis than the nor-methyl tosylate (142),⁴⁹ the rate constants relative to cyclohexyl tosylate being 1900 and 1200 respectively. It is possible that the difference in these figures is a measure of the anchimeric assistance.

Turning now to Doyle's study of exo-3-bicyclo(3.3.2)decyl tosylate (151), from the observed 42-48% hydride shift we would expect considerable anchimeric assistance. Nevertheless, using a Foote-Schleyer correlation^{106,156} Doyle was able to rule out any large degree of participation.³⁵ However,

unaccountably, the carbonyl stretching frequency for 3-bicyclo(3.3.2)
 decanone (152) was wrongly measured; Doyle quotes a figure of
 1698cm.⁻¹; the figure obtained from Doyle's own high resolution
 spectrum is 1693cm.⁻¹, while a series of spectral determinations on
 different spectrophotometers give values between 1692cm.⁻¹ and 1690cm.⁻¹
 If we assume a value of 1692cm.⁻¹ and apply the Foote equation

$$\log k_{rel} = -0.132(\nu_{C=O} - 1720)$$

we obtain a calculated log k_{rel} of 3.70, corresponding to a k_{rel} of
 5000, whereas the observed k_{rel} is 9000. From the data quoted by
 Curisson,¹⁴⁸ this is the order of rate increase that might be expected
 during solvolysis of exo-3-bicyclo(3.3.2)decyl tosylate (151).

If we now apply the rather more complete Schleyer equation¹⁵⁶

$$\log k_{rel} = \frac{1}{8}(1715 - \nu_{C=O}) + 1.32(1 + \cos 3\phi) + \frac{1}{1.36}(GS - TS)$$

in which the first term is again a function of the carbonyl stretching
 frequency and thus of angle strain; the second term is a function of
 the dihedral angle between the tosyloxy group and the β -hydrogens, and
 thus of torsional strain and the third term is a function of the
 difference in non-bonded strain between ground state and transition
 state.

For the first term, if $\nu_{C=O} = 1692$, we have a value of 2.88. For
 the second term, if we assume that the ring geometry in the tosylate
 is similar to that found by NMR for 3-bicyclo(3.3.2)decanone, we get a
 value for the dihedral angle ϕ of about 30° instead of the 50° assumed
 by Doyle, which leads to a value of 2.64 for the second term. For the

final term Doyle estimated a value of 1.5. These three figures lead to a calculated $\log k_{rel}$ of 7. Negative deviations from the Foote-Schleyer correlations are rare, though they have been observed for 4-homoadamantyl tosylate (152), ⁶¹ 2-mantyl tosylate (153) ³⁵ and 9-bicyclo(3.3.2)decyl tosylate (154). ¹⁵⁷ No explanations have been forthcoming for these results, except in the 4-homoadamantyl case where ⁶¹ Schleyer considers that steric hindrance to ionisation occurs. In the case of 3-bicyclo(3.3.2)decyl tosylate, it is remarkable that such a reactive tosylate is still reacting a thousand times slower than calculated. However, it is possible that the torsional and transannular strains have been over estimated.

It is thus not at all clear whether there is in fact participation in the ionisation of exo-3-bicyclo(3.3.2)decyl tosylate. By Ourisson's criteria described above, it is quite likely that a kinetic deuterium isotope effect could be observed in the solvolysis of 7,7-dideutero-exo-3-bicyclo(3.3.2)tosylate (155) which could be prepared by routine methods from bicyclo(3.3.2)decan-3,7-dione monoketal (156).

The synthesis of the ketalketone (156) precursor, 2,4-bis-carbo-methoxybicyclo(3.3.2)decan-3,7-dione (157) was attempted by condensing equivalent amounts of dimethyl acetone-1,3-dicarboxylate (158) with cyclohepta-2,6-dienone (159). Only starting material was recovered from the reaction using a variety of conditions, and a thorough examination of this synthetic route by ¹⁵⁸ halojdic failed to yield any of the required compound (157).

Nevertheless, from the foregoing discussion, it is abundantly clear that the 3-bicyclo(3.3.2)decyl system is a very interesting one, and while Doyle's single study on exo-3-bicyclo(3.3.2)decyl tosylate solvolysis is illuminating in terms of the hypothesis that hydride shifts are governed to some extent by strain and flexibility in the reacting molecule, the hypothesis would be strengthened by further examples of hydride shifts being more facile in the bicyclo(3.3.2)decane system. Because the thorough work by ¹⁵Marvell on the solvolysis of exo-2,3-epoxybicyclo(3.3.1)nonane (136) was available for comparison, as well as Cope's work on cyclo-octene oxide, ¹² it appeared that a solvolytic study of exo-2,3-epoxybicyclo(3.3.2)decane would furnish useful information on this problem.

Marvell subjected exo-2,3-epoxybicyclo(3.3.1)nonane (136) to trifluoroacetylolysis and buffered acetylolysis. Trifluoroacetylolysis gave after hydrolysis of the intermediate trifluoroacetate esters, a mixture of exo-2-hydroxybicyclo(3.3.1)non-6 & 7-ones (160 & 161) in the ratio 80:20. Buffered acetylolysis gave, after lithium aluminium hydride reduction of the intermediate acetates, a mixture of unsaturated alcohols and diols. The unsaturated alcohols were found to be exo-2-hydroxybicyclo(3.3.1)non-6 & 7-ones (160 & 161) (23%), exo-2-hydroxybicyclo(3.3.1)non-3-ane (162) (21%), and a third alcohol, assigned as exo-3-hydroxybicyclo(3.3.1)non-6-ene (163) (3%), though

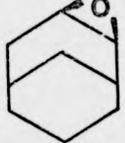
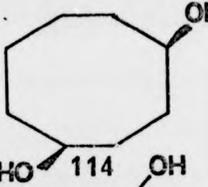
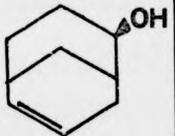
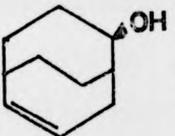
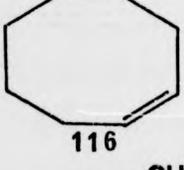
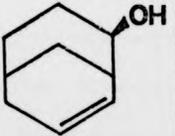
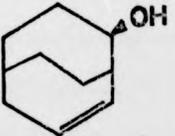
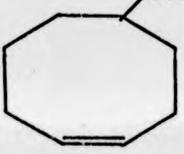
without supporting chemical evidence. The diol fraction consisted of exo-2-endo-3-bicyclo(3.3.1)nonandiol (164) (46%), exo,exo-bicyclo(3.3.1)nonan-2,7-diol (165) (5%) and a third diol (2%) assigned, again with little evidence, as endo-2-exo-3-bicyclo(3.3.1)nonandiol (166). These results are summarised in Tables 1 and 2 (below).

It is clear that since the hydride shift in the trifluoroacetolysis is 100%, trifluoroacetolysis of exo-2,3-epoxybicyclo(3.3.2)decane (21) is unlikely to furnish useful information about the mechanism of hydride shifts. However, the expected product, exo-2-hydroxybicyclo(3.3.2)dec-6(7)-ene (167) would be needed for comparison with the product of buffered acetolysis. Further, this reaction promised to be the first synthesis of a bicyclo(3.3.2)decane derivative substituted in both rings. Therefore, exo-2,3-epoxybicyclo(3.3.2)decane, prepared as described in Chapter 1, was treated with trifluoroacetic acid under the conditions described by Marvell. After hydrolysis of the intermediate trifluoroacetate esters, work up furnished a solid unsaturated alcohol, which, though homogeneous to ordinary GLC columns, was resolved into two components in the ratio (27:73) on a 50m. TCEP capillary column. Marvell's experience suggested that the minor component was exo-2-hydroxybicyclo(3.3.2)dec-7-ene (168) and the major component exo-2-hydroxybicyclo(3.3.2)dec-6-ene (169). For comparison, exo-2-hydroxybicyclo(3.3.2)dec-3-ene (170) was prepared by allylic oxidation of 2-bicyclo(3.3.2)decene with selenium dioxide; though this compound (170) had an identical retention time on GLC with the trifluoroacetolysis

product, and even on the capillary column it had the same retention time as the minor trifluoroacetolysis product, its spectral properties were quite different from those of the trifluoroacetolysis product.

Both the allylic alcohol (170) and the trifluoroacetolysis product were then oxidized to the corresponding ketones. Initially this proved troublesome, the method of Jones ⁹² giving very poor yields; but ⁹³ treatment of an ice cold ethereal solution of the alcohol with Jones chromic acid for one hour furnished the required ketones in excellent yield. The allylic alcohol (170) furnished an α,β -unsaturated ketone (171) which was quite different from the ketones obtained from the trifluoroacetolysis product, both by GLC and by spectral comparison. No bicyclo(3.3.2)dec-2-one-3-ene (171) could be detected in the oxidised trifluoroacetolysis product; hence hydride shift occurred to the extent of 100%. The 100MHz. NMR spectrum of the ketones from the trifluoroacetolysis product was found to have a resonance at 6.94τ integrating for 30% of one proton. This signal was assigned to the proton at position 1 in bicyclo(3.3.2)dec-2-one-7-ene (172) thus establishing this as the minor component of the ketone mixture, and therefore exo-2-hydroxybicyclo(3.3.2)dec-7-ene (168) had to be the minor alcohol in the original product. Wolf-Kishner reduction of the ketone mixture furnished only 2-bicyclo(3.3.2)decene, and no 9-bicyclo(3.3.2)decene, thus demonstrating that the hydride shift was specific from C3 to C7. Finally, a small portion of the original alcohol mixture was reduced catalytically; the sole product was exo-2-bicyclo(3.3.2)decanol, thus

Table 1
Trifluoroacetylolysis of Epoxides

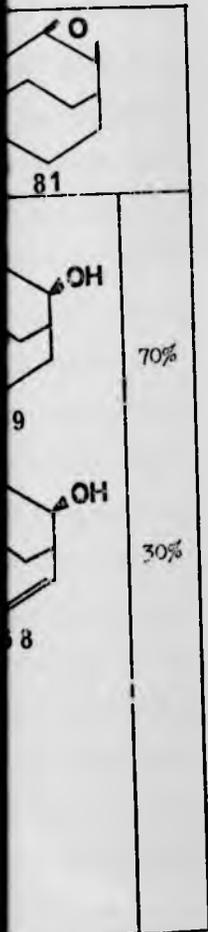
 113		 136		 81	
 114	45%	 160	80%	 169	70%
 116	30.5%	 161	20%	 168	30%
 117	3.5%				

proving the exo con
 that the sole produ
 (3.3.2)decane (81)
 (168 & 169) in the
 Table 1, together w
 and bicyclo(3.3.1)

Attention ther
 procedure was carri
 air and eliminate
 examined by GLC (2
 which were present
 component, had the
 (3.3.2)dec-5(7)-ene
 components were of

An attempt to
 chromatography was
 eluted from a prep
 phase (CVI), while
 tendency to form a

As a result th
 acetate fraction w
 gel. The infra-red
 formed from the tr



proving the exo configuration of the hydroxyl group. It was thus shown that the sole products of trifluoroacetylolysis of exo-2,3-epoxybicyclo(3.3.2)decane (81) were exo-2-hydroxybicyclo(3.3.2)dec-6 & 7-enes (168 & 169) in the ratio $70 \pm 5 : 30 \pm 5$. These results are collected in Table 1, together with the corresponding results from the cyclo-octane and bicyclo(3.3.1)nonane systems.

Attention then turned to acetylolysis of the epoxide (81); this procedure was carried out at 100° in a sealed tube, so as to exclude air and eliminate tar formation. The product of the reaction was examined by GLC ($2\frac{1}{2}\%$ OV1, 180°). This showed six components, three of which were present to the extent of 5% or more. The major (47%) component, had the same retention time as both exo-2-acetoxybicyclo(3.3.2)dec-6(7)-ene (173) and the allylic acetate (174). All the other components were of longer retention times.

An attempt to separate the components by preparative gas chromatography was unsuccessful, as the more polar components were not eluted from a preparative column containing as little as 7% stationary phase (CV1), while the compounds that were eluted showed a remarkable tendency to form aerosols which could not be condensed.

As a result the reaction product was separated into an unsaturated acetate fraction and a diacetate fraction by chromatography on silica gel. The infra-red spectrum was very similar to that of the acetates formed from the trifluoroacetylolysis product (173) and was different from

that of the allylic acetate (174). GLC analysis on the 50m. MEG capillary column resolved the mixture into four components, which were identified by cross injection with known samples as: unknown (3%); exo-2-acetoxycyclo(3.3.2)dec-7-ene (175) (37%); exo-2-acetoxycyclo(3.3.2)dec-6-ene (176) (50%); and exo-2-acetoxycyclo(3.3.2)dec-3-ene (11%) (174). Reduction of the unsaturated acetate mixture with lithium aluminium hydride and GLC analysis of the resulting alcohols showed: unknown (3%); exo-2-hydroxycyclo(3.3.2)dec-6-ene (169) (49%); and exo-2-hydroxycyclo(3.3.2)dec-3(7)-ene (168 & 170) (48%). Catalytic reduction of the alcohol mixture gave an unknown (3%) and exo-2-bicyclo(3.3.2)decanol (97%). The unknown at this stage was not exo-2, exo-3,1- or 9-bicyclo(3.3.2)decanol. It is perhaps possible that it could be endo-2- or endo-3-bicyclo(3.3.2)decanol, but this would be very unlikely, as such a product would have to arise from an endo-epoxide and thus should have been observed in the trifluoroacetolysis product. Another possibility is that it could be the product of a trans-annular ring closure, to tricyclo(3.3.2.0^{3,7})dec-2-yl acetate (177). Such a process is known to occur during the acetolysis of exo-norbornene oxide (173),¹⁵⁹ and this assignment is strengthened by the observation that the retention time of the unknown did not alter after catalytic reduction of the acetolysis product.

An attempt was made to synthesise exo-2-tricyclo(3.3.2.0^{3,7})
decanol (181) by the treatment of exo-2,3-epoxycyclo(3.3.2)decane

(81) with lithium diethylamide; this gives solely the ring closed product, 2-nortricyclanol (179) from *exo*-norbornene oxide (178),¹⁵⁹ and mainly the ring closed product, *endo*, *cis*-2-bicyclo(3.3.0)octanol (180) from *cis*-cyclo-octene oxide.¹³³ In the event, the sole product was found to be the allylic alcohol (170), identical with a sample as previously prepared. Oxidation gave the previously prepared α,β -unsaturated ketone (171).

This initially surprising result in fact furnishes convincing evidence in favour of Grandall's¹⁶⁰ theories concerning the action of strongly basic, non-nucleophilic reagents on epoxides. Two separate elimination pathways appear to operate in these reactions; a) a β -elimination pathway giving rise to an allylic alcohol, and b) an α -elimination pathway giving rise to a carbenoid intermediate, which then undergoes transannular ring closure. The ratio of products formed by the two routes is dependant on structural and conformational factors; thus norbornene oxide cannot undergo a β -elimination pathway. It appears that the decisive feature which controls the balance between these two reaction pathways is the stereoelectronic requirement for β -elimination. Thus molecules existing mainly or exclusively in conformations capable of undergoing β -elimination by a *trans-anti-parallel* arrangement of one of the carbon oxygen bonds of the epoxide ring and a proton on an adjacent carbon atom will do so readily. Thus, cyclopentene, cyclohexene and cyclododecene oxides all give rise to the allylic alcohol in preparatively useful yields. Particularly significant is that α -pinene oxide (182)¹⁶⁰ gives rise only to pinocarveol (183), with an exocyclic double bond,

rather than the isomer with an endocyclic double bond (184). Only elimination from the methyl group in α -pinene oxide gives rise to the required atomic arrangement for β -elimination.

By contrast, in medium rings transannular products predominate, and Crandell¹⁵⁰ suggests that this is due to inhibition of the normal elimination process imposed by the scarcity of the required reaction site conformations for β -elimination. As a result, the normally less favoured α -elimination process occurs instead.

If we look at a molecular model of cis-cyclo-octene oxide in the now proven boat chair conformation,¹²³ it is seen that the conformation for β -elimination at the epoxide ring is quite strained, and so the reaction proceeds mainly by the α -elimination pathway. However, in the case of exo-2,3-epoxybicyclo(3.3.2)decane, the eight membered ring is now constrained by the two carbon bridge into a favourable conformation for β -elimination; and thus, although this is a strained conformation, it is now less strained rather than more strained. Therefore the allylic alcohol (170) is the sole product of the reaction of exo-2,3-epoxybicyclo(3.3.2)decane with lithium diethylamide.

Attention then turned to the diacetate fraction from the buffered acetolysis. GLC showed two major components (20% and 17% of the product mixture) and three minor components (4%, 1% and 1%). Isolation of the two major components only proved practicable; this was carried by chromatography on silica gel. The infra red spectra confirmed that the compounds were diacetates, but furnished no further information.

However, there was a striking difference in the NMR spectra; the carbonyl protons of the less polar, 20% component exhibited resonances integrating for 2 protons at approximately 5 τ . This consisted of a seven line multiplet with splittings of 5Hz. and 11Hz., similar to that observed for exo-3-bicyclo(3.3.2)decanol, with a sharp narrow resonance superimposed. The strongly coupled signal was thus assigned to the carbonyl proton next to a 7-acetoxy group. The field position of the signal is considerably higher than expected for an exo-7-acetoxy group, and a little lower than expected for an endo-7-acetoxy group.
15
However, Harvell reports no transannular deshielding of the endo-7-proton in exo,exo-bicyclo(3.3.1)nonan-2,7-diol (165), and so because of this, together with the fact that an endo attack at C7 is unlikely this signal is assigned as arising from the proton adjacent to an exo-7-acetoxy group. Such a substitution pattern could, in any case, only arise via a hydride shift route. The narrow resonance is presumably the carbonyl proton adjacent to the exo-2-acetoxy group. The acetate signal (8.02 τ) integrates for six protons. Thus this component is assigned as exo,exo-2,7-diacetoxycyclo(3.3.2)decane (185). The more polar, 17% component showed much less structure in the carbonyl proton resonance (approx. 5 τ), which again integrated for 2 protons. No coupling constants could be extracted as it was a broad, complex band of 18Hz. width at half height. Such a band width is too wide for equatorial protons, unless the two bands were side by side. exo-2-endo-3-Diacetoxycyclo(3.3.2)decane (186), would be expected from the solvolysis; this compound would be expected to exist in a

boat-chair conformation with the acetoxy groups on the boat part of the molecule. In this case, both the carbinyl protons will be homo-axial, with quite large couplings, and since these protons will form the AB part of an ABXY system their resonance signals would be expected to be very complex. It is thus reasonable to assign this structure (186) to the 17% component of the mixture.

To confirm these assignments, the diacetates were reduced to the corresponding diols with lithium aluminium hydride. The solid phase infra red spectra and the NMR spectra were no more informative than the original acetate spectra.

A sample of the diacetate mixture was reduced with lithium aluminium hydride to the corresponding diol mixture which was then treated with acidic potassium periodate. After oxidation of the reaction product with hydrogen peroxide and extraction of acidic material with sodium bicarbonate, a solid product was obtained. Thin layer chromatography showed that this was the diol assigned as exo,exo-bicyclo(3.3.2) decan-2,7-diol (187). The diol assigned as exo-2-endo-3-bicyclo(3.3.2) decandiol (188) which was present before treatment with periodate was no longer present. This proves that the more polar, 17% diol is a vicinal diol while the less polar, 20% diol is a non-vicinal diol.

While there is thus no complete proof of the respective structures of these diacetates and diols in the absolute sense, the chemical and spectral evidence is consistent with the formulations, which are the main expected products. There is as yet no evidence as to the nature of the minor products; GCMS would be a useful first step as this would show

Table 2
Acetolysis of Epoxides

113		136		81	
	7.5%		21%		6.5%
	2.5%		23%		23.5%
	71%			?	
	9%		46%		17%
others	3%		5%		20%
			?	A	4%
			2%	B	1%
				C	1%

if they were degra
2% component of th
after reduction to
(166), as it was r
2,3-diol (189), bu

The results of
12
Cope and Marvell

shifts occur to a
decane system than
striking is the di
in the bicyclo(3.3.2)
5% of the total p
bicyclo(3.3.2)dec
total products or
only 6.5% of allyl
system as against

The percenta
follows:- in the
nonane system, 10
alcohol fractions
system, 49%; bicy

These results
Doyle's results
constitute grati
and flexibility of

	81	
	0	6.5%
	9	23.5%
	8	17.5%
	8	1.5%
	8	17%
	8	20%
	87	4%
	B	1%
	C	1%

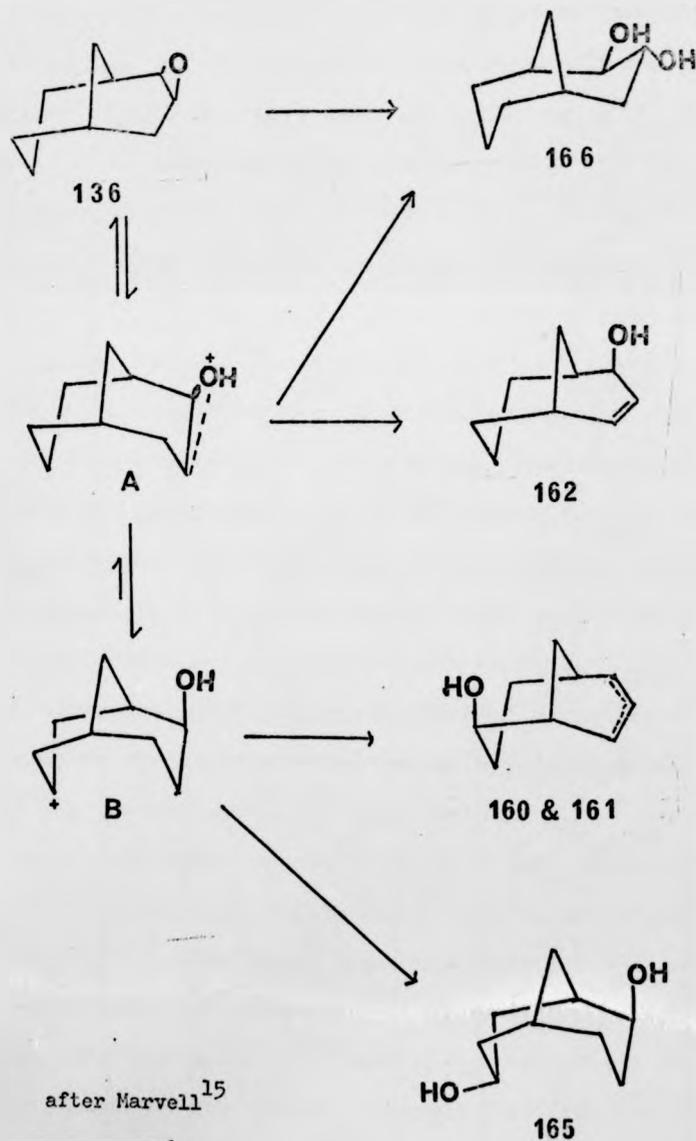
if they were degradation products or not. Marvell suggested that the 2% component of the exo-2,3-epoxybicyclo(3.3.1)nonane acetolysis might, after reduction to the diol, be endo-2-exo-3-bicyclo(3.3.1)nonandiol (166), as it was neither the exo-2-endo-3-diol (164) nor the exo,exo-2,3-diol (189), but it was cleaved by periodate.

The results of this acetolysis study, together with those of Cope and Marvell are summarised in Table 2. It is clear that hydride shifts occur to a significantly greater extent in the bicyclo(3.3.2)decane system than in the bicyclo(3.3.1)nonane system. Particularly striking is the difference in the amount of transannular diols formed; in the bicyclo(3.3.1)nonane system, transannular diol constituted only 5% of the total product, or 11% of the diol fraction, while in the bicyclo(3.3.2)decane system, transannular diol constitutes 20% of the total products or 48% of the diol fraction. In accordance with this, only 6.5% of allylic alcohol is formed in the bicyclo(3.3.2)decane system as against 21% in the bicyclo(3.3.1)nonane system.

The percentage of hydride shifts in the three systems are as follows:- in the diol fractions; cyclo-octane system, 10%; bicyclo(3.3.1)nonane system, 10%; bicyclo(3.3.2)decane system, 48%; in the unsaturated alcohol fractions; cyclo-octane system, 85%; bicyclo(3.3.1)nonane system, 49%; bicyclo(3.3.2)decane system, 89%.

These results may not be particularly surprising in view of Doyle's results from exo-3-bicyclo(3.3.2)decyl tosylate, but they constitute gratifying supporting evidence for the theory of a distance and flexibility effect being a significant factor in transannular

Scheme 3



hydride shift nec

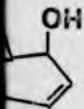
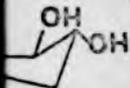
As pointed o
hydrogens in the
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hydride shift mechanisms.

As pointed out in Chapter 1, the distance between the endo hydrogens in the twin chair conformation of bicyclo(3.3.2)decane is estimated at 200 ± 20 pm., while the equivalent distance in bicyclo(3.3.1)nonane is 180 pm.; though a Droiding model predicts a smaller distance for bicyclo(3.3.2)decane. This shows that the ground state interhydrogen distance is not important for hydride shifts; what is important is the distance that can be achieved in a high energy transition state, and in a more flexible system such as bicyclo(3.3.2)decane a smaller distance is more easily achieved, and so hydride shift is facilitated.

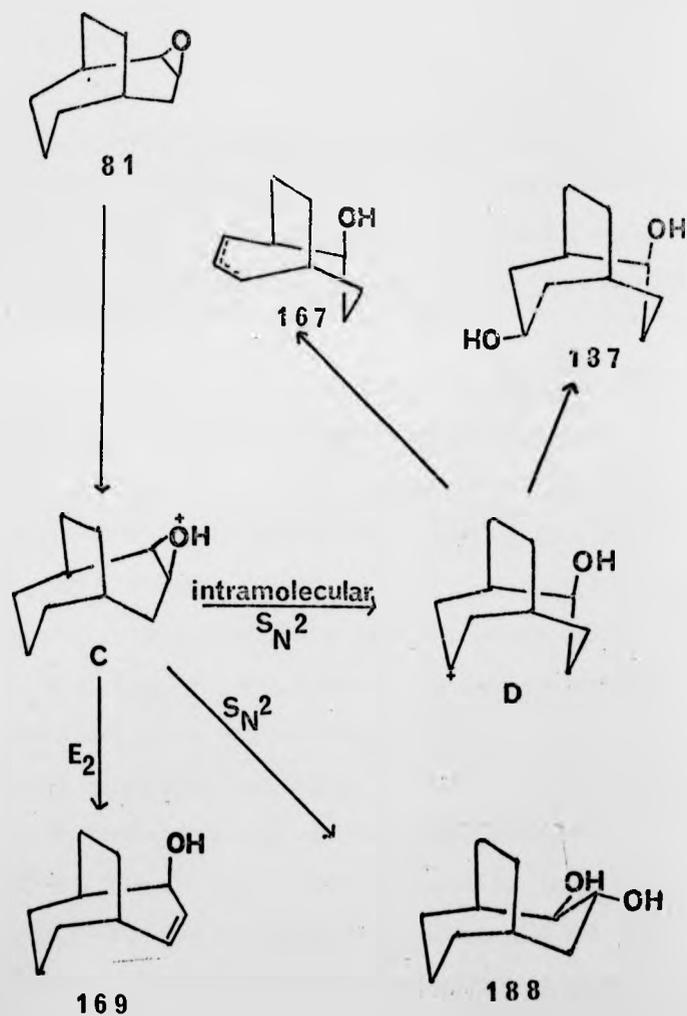
How much light do these results show on the question of whether the hydride shift is fully or partially concerted with either the ionisation, or the elimination, or the counter ion capture? One factor that other reaction schemes for hydride shifts in epoxide solvolysis have never satisfactorily accounted for is the different extents to which hydride shifts occur in different reaction pathways of the same initial cation. Thus, if we look at Cope's scheme (scheme 1) for the solvolysis of cyclo-octene oxide, or perhaps more relevantly, Marvell's scheme¹² for the acetolysis of exo-2,3-epoxybicyclo(3.3.1)nonane (scheme¹⁵ 3) there is no explanation of why ion A should be more likely to react by counter ion capture, while ion B is more likely to take an elimination pathway. The explanation cannot be steric - indeed stereochemical considerations would militate against that idea, as formation of the



161



Scheme 4



trans vicinal diol process; whereas steric constraints of a bicyclo(3.3.1) considerations re counter ion capture

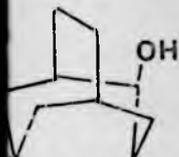
Further, the absence of any allylic nor for the absence of a carbonium ion intermediate to an enol as to

It appears, an intermediate exists and that the mechanism is better. Here the classical carbocation is the oxonium ion. This has, in principle, the allylic alcohol intramolecular S_N2 carbonium ion **D**, products, and only. The scheme satisfies with trifluoroacetic

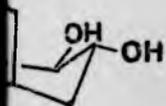
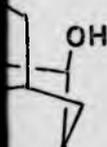
trans vicinal diol, by endo attack, must be a relatively hindered process; whereas elimination of a proton should not be so subject to steric constraints. The observed reactivity of ion B is fairly typical of a bicyclo(3.3.1)nonyl carbonium ion at position 3 or 7; strain considerations result in elimination products being favoured over counter ion capture products.

Further, these reaction schemes do not account for the total absence of any allylic alcohol during epoxide trifluoroacetylolysis, nor for the absence of ketonic products, which would be expected from a carbonium ion such as A in scheme 4, which could as easily eliminate to an enol as to an allylic alcohol.

It appears, therefore, that the evidence for a carbonium ion intermediate existing before hydride shift has taken place is poor, and that the mechanistic scheme (scheme 4) fits the observed facts better. Here there is no suggestion of either a classical or a non-classical carbonium ion being the initial reacting species. Rather it is the oxonium ion C, formed by protonation of the epoxide ring. This has, in principle, three reaction pathways open to it; E2 to give the allylic alcohol; S_N2 to give the trans vicinal diol, and an intramolecular S_N2 by the migrating hydride, to give a classical carbonium ion D, which reacts as expected to give mainly elimination products, and only a small proportion of counter ion capture products. The scheme satisfactorily explains the observed 100% hydride shift with trifluoroacetic acid, since the nucleophilicity of the conjugate



137



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base of this acid is insufficient to open the oxonium ion by an S_N2 mechanism, nor is the conjugate base strong enough to remove the proton in an $E2$ mechanism. Therefore, the only available reaction pathway is by intramolecular S_N2 by migrating hydride, and so there is 100% hydride shift. Further, this mechanism could not give rise to any ketonic products, by elimination from a carbonium ion to give an enol.

A mechanism such as scheme 4 has presumably always been ruled out before by the absence of kinetic isotope effects during arenesulphonate solvolysis.^{12,15} However, there is no valid reason why the mechanism of epoxide solvolysis should parallel that of tosylate solvolysis, and since Curisson^{148,149} has demonstrated transannular hydride participation in tosylate solvolysis, albeit systems in which the migration is from a secondary to a tertiary centre, the above scheme seems less unlikely. It is noteworthy that Curisson's¹⁴⁹ preferred mechanism for transannular hydride participation is an intramolecular S_N2 reaction as suggested here.

There is one remaining observation to account for; viz. the rather surprising fact that the transannular elimination product from trifluoroacetolysis of *exo*-2,3-epoxybicyclo(3.3.2)decane, is 70% the 2,6-isomer (169) and 30% the 2,7-isomer (168); while from acetolysis the amounts of the two alcohols are more nearly equal, 57% of the 2,6-isomer (169) and 43% of the 2,7-isomer (168). The explanation is by no means obvious; it is possible that the 2,6-isomer (169) is slightly more stable than the 2,7-isomer (168), and in the more strongly

acid medium of trifluoroacetic acid, the carbonium ion D in scheme 4 will be longer lived, and thus more likely to react to give the more stable product. In any case, before one can make any meaningful rationalisations on this problem, a thorough examination of the stability of the various reaction products to the solvolysis conditions, and of the stability of, say, the acetolysis product to the trifluoroacetolysis conditions will be necessary.

By these studies on solvolysis of exo-2,3-epoxybicyclo(3.3.2)decane we have cleared the air surrounding the problems of hydride shift mechanisms a little further. Thus we have shown a) the importance of the distance that can be achieved in the transition state between the potentially migrating hydride and the reacting centre, without incurring prohibitive ring strain; and b) the probability of participation by the migrating hydride in the opening of an epoxide ring.

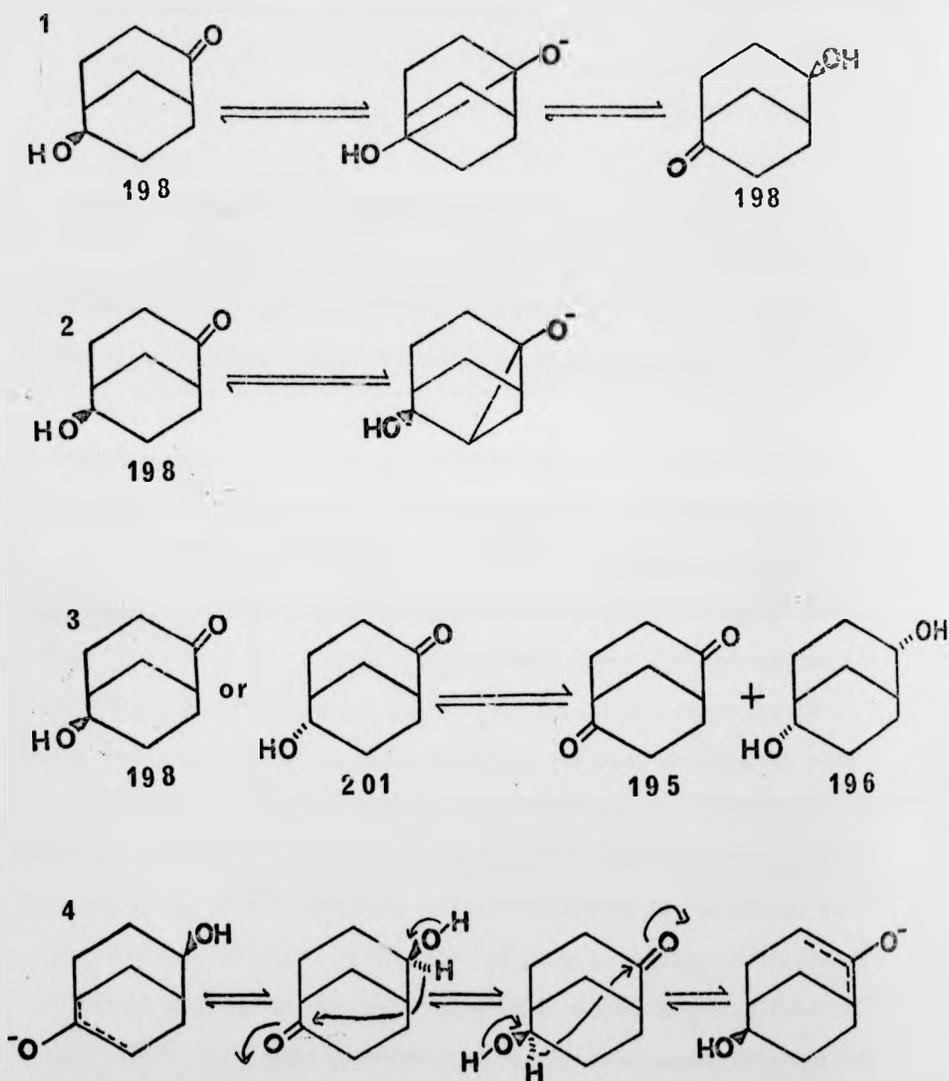
3,7-Hydride shifts in the bicyclo(3.3.1)nonane system are well established, and now it is clear that in the bicyclo(3.3.2)decane system this process is even more facile. At the same time as carrying out these studies into systems giving rise to reaction at position 3, it seemed advisable to examine position 2 as well. Processes involving a direct 2,6-interaction in the twin-twist-boat conformation of bicyclo(3.3.1)nonane (the configuration required for such an interaction) are much less well documented. Indeed, there has been indirect evidence for twin-twist-boat conformations of bicyclo(3.3.1)nonane derivatives from only two studies.

Marshall and Faubl postulated the intermediacy of the twin-twist-boat conformation of endo-2-methanesulphonyloxybicyclo(3.3.1)nonane-1-carboxylic acid (193) during elimination to give 1-bicyclo(3.3.1)nonane (194), since only this conformation will provide the stereoelectronically required trans-antiparallel arrangement.

Schaefer and Honig obtained two alcohols from sodium borohydride reduction of bicyclo(3.3.1)nonan-2,6-dione (195), which were assumed to be the endo,endo- (196) and the endo,exo- (197) bicyclo(3.3.1)nonan-2,6-diols, though the stereochemistry was not proven. The rationale for the formation of the endo,exo-epimer (197) was that the initially formed alkoxyborohydride produced by preferential exo attack of the hydride assumed the twin-twist-boat conformation before reduction of the second carbonyl group from the endo face.

It was these two postulates of 2- and 2,6-substituted bicyclo(3.3.1)nonane derivatives reacting in twin-twist-boat transition states which caused Stevenson ^{50a} to examine the possibility of observing 2,6-hydride shifts and detecting neighbouring group participation between positions 2 and 6; and he did indeed discover a 2,6-hydride shift in the bicyclo(3.3.1)nonane system. During base induced deuteration, exo-2-hydroxy bicyclo(3.3.1)nonan-6-one (198) took up six deuterium atoms instead of the expected three, whereas the corresponding endo-epimer (201) only incorporated three deuterium atoms. If the hydride shift had been a sequence of 2,3-, 3,7-, 7,6-hydride shifts, the deuterium would be incorporated at position 2 but not at position 1. In fact, no deuterium

Scheme 5



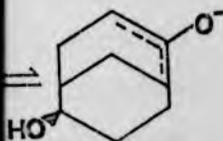
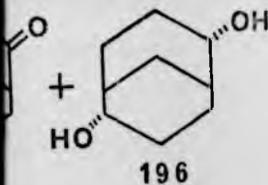
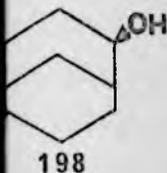
- 1) Homoenolisation at C2.
- 2) Homoenolisation at C3.
- 3) Disproportionation.
- 4) 2,6-Hydride shift.

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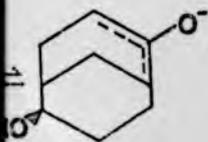
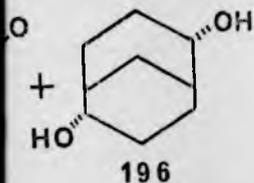
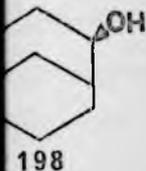


was incorporated at position 2 (as shown by NMR). Another alternative mechanism would have been homoenolisation, but Stevenson's experimental conditions were much less drastic than those required to bring about homoenolisation of camphenilone (193),¹⁶⁴ and homoenolisation at position 2 would require incorporation of seven deuterium atoms instead of the observed six, and that seventh deuterium would be at C2, and, as already noted, C2 was found to be free of deuterium incorporation. Correspondingly, homoenolisation at position 3 would require uptake of only 5 deuterium atoms.

Yet another possibility was a bimolecular disproportionation reaction in which the two molecules of ketol (198 or 201) are transformed into one of the dione (195) and one of the diol (200). However, the exo-ketol (198) was not converted to the endo-ketol (201) under the reaction conditions, nor was a mixture of the dione (195) and the diol (200) converted, even in part, to either the exo- or the endo-ketol (198 or 201). (All these mechanisms are in scheme 5).

Thus the incorporation result was consistent with, and only with, a stereospecific base induced intramolecular 2,6-hydride shift, presumably occurring via a twin-twist-boat transition state.

Acklin and Prelog¹⁶⁵ have reported a similar 1,5-hydride shift in a hydrindane ketol, namely (1S,8S)-1-hydroxy-8-methyl-cis-hydrindane-5-one (237) which was converted to (5S,8S)-5-hydroxy-8-methyl-cis-hydrindane-1-one (238) on neutral alumina; and Lansbury and Saeva¹⁶⁶ showed that 1-substituted-7-hydroxy-12(7H)-pleiadrenones (239) when treated with



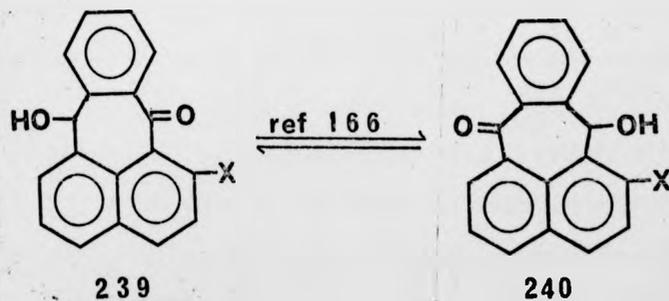
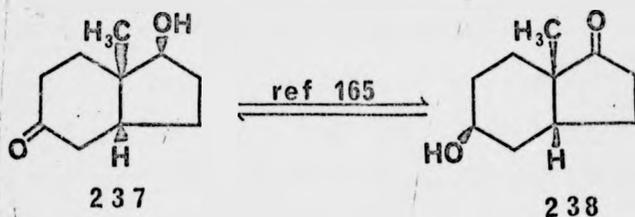
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Fig 4



alkali metal tert.
7(12H)-pleiadenone
allowed Lansbury to
annular hydride shi

These examples
under strongly basic
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solvolytic study
(202 & 203), though
shift had occurred
bicyclo(3.3.1)nonyl
boat conformation;

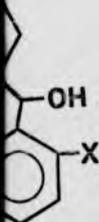
of activation for
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Doyle carried
of the buffered ac
which exhibited cl
reactivity as comp
Interestingly, the
if anything, even
(202) ($k_{\text{rel}}=108$).

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mation was postula
for the high exo:
acetates formed in
2,6-bridged ion in



8



alkali metal tert.-butoxides rearrange to 1-substituted-12-hydroxy-7(12H)-pleiadenones (240). Indeed, it is this last result which allowed Lansbury to put a figure on the activation energy for a transannular hydride shift of approximately 100 kJ_{mol}⁻¹. (See Fig. 4).

These examples, though extremely interesting, were carried out under strongly basic equilibrating conditions. Penrose, in his solvolytic study⁹⁶ of the exo- and endo-2-bicyclo(3.3.1)nonyl tosylate (202 & 203), though he was not in a position to tell if any hydride shift had occurred during the solvolyses, did consider that endo-2-bicyclo(3.3.1)nonyl tosylate (203) was solvolysing via a twin-twist-boat conformation; this was to explain the unexpected positive entropy of activation for the solvolysis.

Doyle³⁵ carried out a kinetic study and partial product analysis of the buffered acetolysis of exo-2-bicyclo(3.3.2)decyl tosylate (204), which exhibited clean first order kinetics and a dramatically reduced reactivity as compared with exo-3-bicyclo(3.3.2)decyl tosylate (151). Interestingly, the rate (relative to cyclohexyl tosylate, $k_{rel}=93$) is, if anything, even slower than for exo-2-bicyclo(3.3.1)nonyl tosylate (202) ($k_{rel}=108$). The absence of any dramatic anchimeric assistance was inferred from the good agreement of the observed rate constant with that¹⁰⁶ calculated from the Foote relation. Again, a twin-twist-boat conformation was postulated as a possible intermediate, in this case to account for the high exo:endo ratio observed for the 2-bicyclo(3.3.2)decyl acetates formed in the reaction, formed by counter ion capture by a³⁵ 2,3-bridged ion in a twin-twist-boat conformation (218).

Table 2

Buffered Acetolysis of exo-2-Tosylates(%): Products in order of elution from GLC (50m. TCEP capillary)

R=OAc		R=OAc		R=OAc		R=OAc		R=OAc		R=OAc		R=OAc		R=OAc		R=OAc		R=OAc		R=OAc	
acetate olefin = 5:95 $k_{rel} = 107$	95	-	-	0.75	-	2.2	1.0	0.75	0.15												
	A	B	C	D	E	F	G														
Olefins	3	6	1	10	1	65	0.2	0.2	0.2												
Acetates	H	I	J	K	L																
acetate = olefin = 14:86 $k_{rel} = 93$	2.1	0.2	0.1	0.1	0.2	5.6	5.4	0.4	0.6	0.4											
																					-

On account of
solvolysis of exo-2
particularly with a

Doyle's incomple
increased acetate:ole
as compared with exo
5:95. The main ole
present to the exte
are three other maj
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other hydrocarbon c
by Doyle. There ar
extent of approxima
bicyclo(3.3.2)decyl
the other as an un
(206). A comparat
2.1%, and the other
of between 0.5 and
(207 & 208), and e
no 9-bicyclo(3.3.2)
quantities of at l
reported by Doyle.
with those for exo

The striking

a) the acetate:olefin ratios; b) the high stereospecificity of exo-2-bicyclo(3.3.2)decyl acetate formation; c) the presence of 1-bicyclo(3.3.2)decyl acetate; d) the large number of other olefinic components, which do not appear to have acetate counterparts (in fact, it is probable that acetate counterparts to all the olefins are present, but there will be such small proportions of them as to make them undetectable. The GLC detection limit for the acetates is probably about 0.1%; that for the olefins will be rather smaller because of the shorter retention time and correspondingly narrower peaks, and is of the order of 0.05%. It is also important to note at this point that all the percentage amounts are determined by integration of the GLC trace, and it is probable that the detector response to the olefins will be different to that of the acetates. As a result, the acetate:olefin ratio may be even greater than reported. However, the detector response will be the same for all the olefins and all the acetates, and so the ratios of one acetate to another or one olefin to another are accurate).

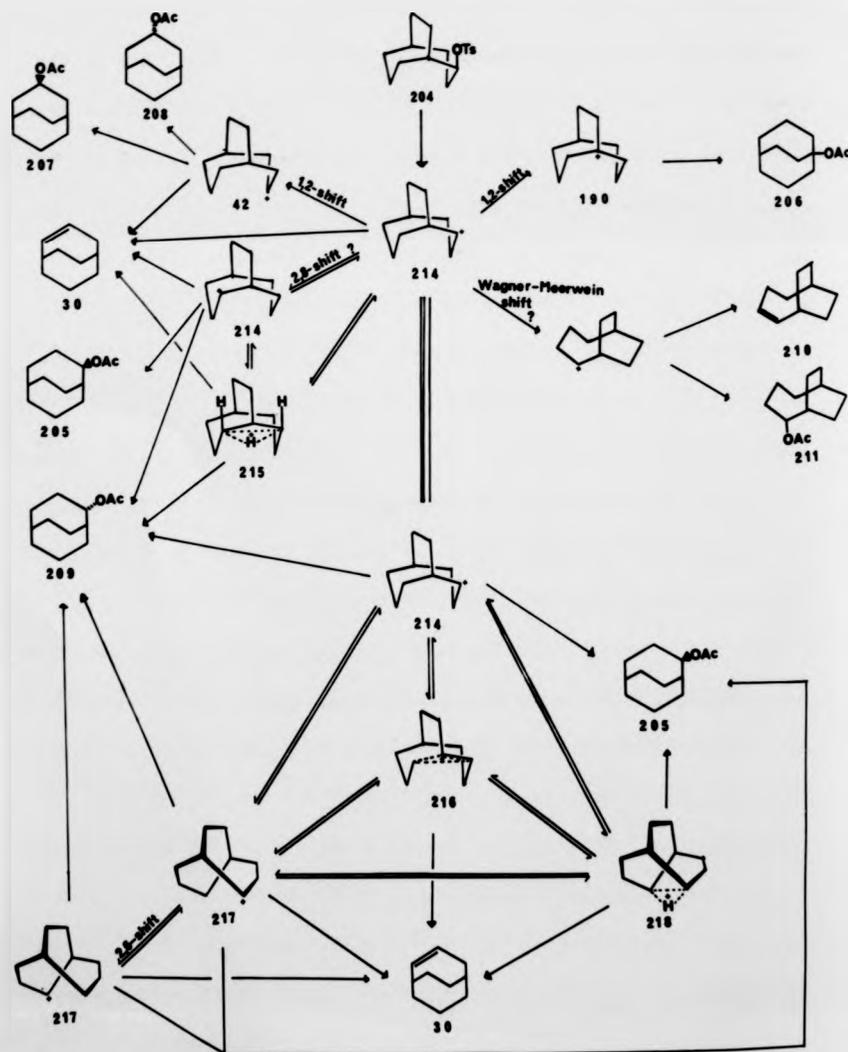
It is probable that the major unassigned olefin (D) and acetate (H) are the Wagner-Beerwein related bicyclo(4.2.2)decane derivatives 2-bicyclo(4.2.2)decene (210) and 2-bicyclo(4.2.2)decyl acetate (211).

The identity of the many other olefinic components is not immediately obvious; although one of them may be 1-bicyclo(3.3.2)decene (212), this anti-Breit olefin would be expected to react with solvent to give 1-bicyclo(3.3.2)decyl acetate (206), since 1-bicyclo(3.3.1)nonene (194) reacts vigorously with glacial acetic acid at room temperature to

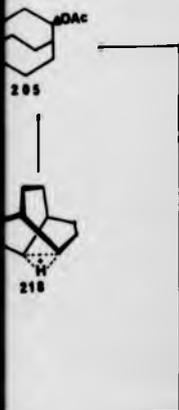
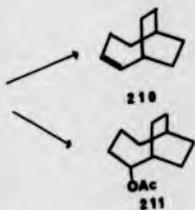
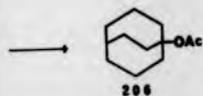
give 1-bicyclo(3.3.1)nonyl acetate (213). Indeed, it is possible that the unprecedented formation of the bridgehead acetate (206) in the solvolysis of exo-2-bicyclo(3.3.2)decyl tosylate is via the anti-Bredt olefin (212), formed by deprotonation of the 2-bicyclo(3.3.2)decyl cation (214). More interesting is the possibility of an intramolecular 1,2-hydride shift to give the bridgehead carbonium ion (190). It is also possible that both processes are occurring, and it would be interesting to prepare 1-bicyclo(3.3.2)decene (212) and examine its stability to the solvolysis conditions. It would also be interesting to see if there is any evidence for 1-bicyclo(3.3.2)decene being formed in other elimination reactions of 2-substituted bicyclo(3.3.2)decene derivatives.

If it is found that the formation of the bridgehead acetate (206) is due, at least in part, to a 1,2-hydride shift to give the bridgehead carbonium ion (190), then this ion must be of at least comparable stability to the 2-bicyclo(3.3.2)decyl carbonium ion (214). That such a process might occur is not, in fact, so surprising, since Schleyer has calculated that there is a strain energy decrease of 10 kJmole^{-1} on going from bicyclo(3.3.2)decane itself to the 1-bicyclo(3.3.2)decyl carbonium ion.⁴⁶ By contrast, in the bicyclo(3.3.1)nonane case, there is a calculated strain energy increase of 35 kJmole^{-1} . It is thus not surprising that there is no 1-bicyclo(3.3.1)nonyl acetate formed in the solvolysis of exo-2-bicyclo(3.3.1)nonyl tosylate; while in the solvolysis of exo-2-bicyclo(3.3.2)decyl tosylate, the bridgehead acetate is formed to a slightly greater extent than exo-2-bicyclo(3.3.2)decyl acetate.

Scheme 6



The explanation
exo-2-tosylates in
 decane systems, viz
 the stereospecific
 bicyclo(3.3.2)decane
 are characteristic of
 35
 noted, Foyle had po
 twist-boat ion (213)
 account for the ster
 Another possible int
 ion (216) which can
 twin-twist-boat con
 the observed stereod
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 (206) and the probab
 (210 & 211), and the
 both militate again
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 consider a reaction
 To check if the
 ions (216) and/or (2
 scrambling in the pu
 reduction of exo-2,
 aluminum deuteride



The explanation of the other two striking differences between the exo-2-acylates in the bicyclo(3.3.1)nonane and the bicyclo(3.3.2)decane systems, *viz.* the comparatively high acetate:olefin ratio and the stereospecificity of the exo-2-acetate (205) formation in the bicyclo(3.3.2)decane system are probably related. Both these properties are characteristic of non-classical ion intermediates, and as already noted, ³⁵ Foyle had postulated the possibility of a 2,6-bridged twin-twist-boat ion (213) as an intermediate in this solvolysis that could account for the stereospecificity of the exo-2-acetate (205) formation. Another possible intermediate is the more conventional non-classical ion (216) which can rearrange to a 2-bicyclo(3.3.2)decyl cation in a twin-twist-boat conformation (217). Both these ions could give rise to the observed stereospecificity. However, the formation of the many other products observed, in particular the 1-bicyclo(3.3.2)decyl acetate (206) and the probable formation of the bicyclo(4.2.2)decane derivatives (210 & 211), and the observed absence of any marked anchimeric assistance both militate against the idea of any non-classical ion being the sole intermediate in the solvolysis reaction. We are therefore compelled to consider a reaction scheme such as scheme 6.

To check if the exo-2-acetate was being formed via the non-classical ions (216) and/or (213), either of which should give rise to a detectable scrambling in the product, a simple labelling scheme was adopted - reduction of exo-2,3-epoxybicyclo(3.3.2)decane (61) with lithium aluminium deuteride furnished endo-3-deutero-exo-2-bicyclo(3.3.2)decanol

(219). The corresponding tosylate (219a) was solvolysed in buffered acetic acid in a sealed tube at 40° for 3 days, a total of 11.5 half lives. After work up, the product was analysed by GLC, and there was no significant difference between the product distribution of this solvolysis and in the unlabelled case; though the exact ratios were not checked, the relative amounts of the various acetates and the olefins other than 2-bicyclo(3.3.2)decene were qualitatively similar in both cases.

The entire reaction product was then treated with lithium aluminium hydride and the resulting olefin/alcohol mixture was treated with Jones' chromic acid. ⁹² GLC analysis at this stage showed the presence of 2-bicyclo(3.3.2)decanone (83) and 1-bicyclo(3.3.2)decanol (14) as the main non-olefinic products, confirmed by cross injection with authentic samples. The product was then treated with a solution of sodium in aqueous dioxane under conditions known to exchange deuterium atoms adjacent to the carbonyl group in 2-bicyclo(3.3.2)decanone. ³⁵ A sample of the product from this washout procedure was then examined by combined GLC-mass spectrometry, which showed that 32% of the 2-bicyclo(3.3.2)decanone in the mixture still contained one deuterium atom.

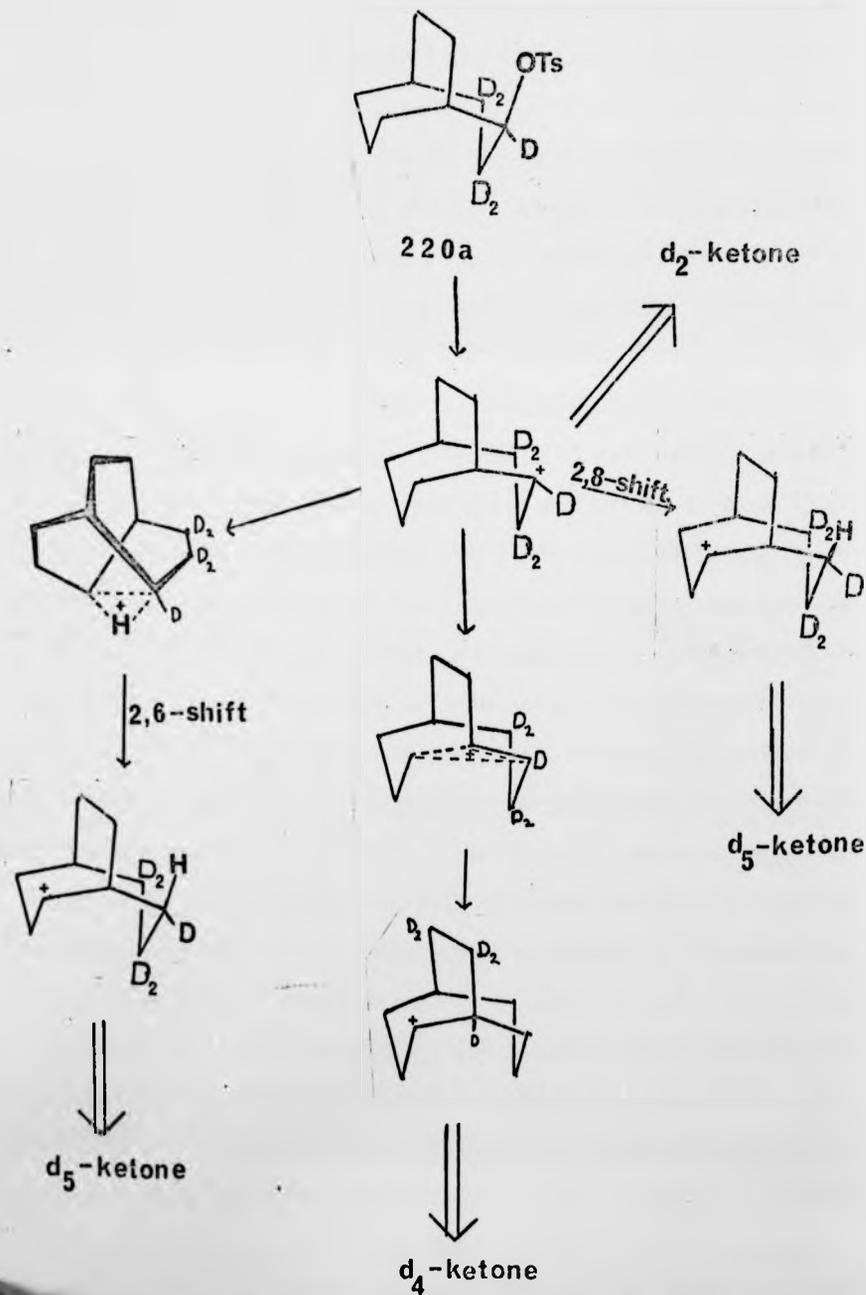
This shows that at least a considerable portion of the exo-2-bicyclo(3.3.2)decyl acetate has been formed by a route resulting in scrambling of the label, either due to the non-classical ion (216) or to a transannular 2,6-hydride shift in the bridged twin-twist-boat ion (217), but this result does not distinguish between these two possible intermediates. Nor is the possibility of a 2,6-hydride shift

in the classical 2-bicyclo(3.3.2)decyl carbonium ion (214) ruled out. A 2,8-bridged twin-chair non-classical ion (215) is an unlikely intermediate as this intermediate would give rise to mainly endo-2-bicyclo(3.3.2)decyl acetate (209). A non-classical ion intermediate (216) could be distinguished from a hydride shift mechanism by more complete labelling, but this would require a much longer synthetic sequence. Neither a non-classical ion nor a 2,6-bridged twin-twist-boat ion have any parallel in the bicyclo(3.3.1)nonane system, as Penrose⁹⁶ in his thorough study of solvolytic relationships in related bicyclononane systems showed that the solvolysis of exo-2-bicyclo(3.3.1)nonyl tosylate was completely classical. A 2,8-hydride shift has been reported for the bicyclo(3.3.1)nonane system, though. Schaefer and Honig¹⁶³ isolated 2-bicyclo(3.3.1)nonanone (85) from the sulphuric acid dehydration of a mixture of endo,endo- and endo,exo-bicyclo(3.3.1)nonan-2,6-diols (196 & 197). By examining the products of dehydration of 3,3,7,7-tetra-deuterated diols, Schaefer and Honig considered that the results were best explained by a sequence of 2,3-, 3,2- and 2,8-hydride shifts, possibly including olefinic intermediates as well. However, the argument is by no means conclusive, and similar products could be obtained by a sequence of 2,3- and 3,7-hydride shifts, with olefinic intermediates; or by a direct 2,6-hydride shift.

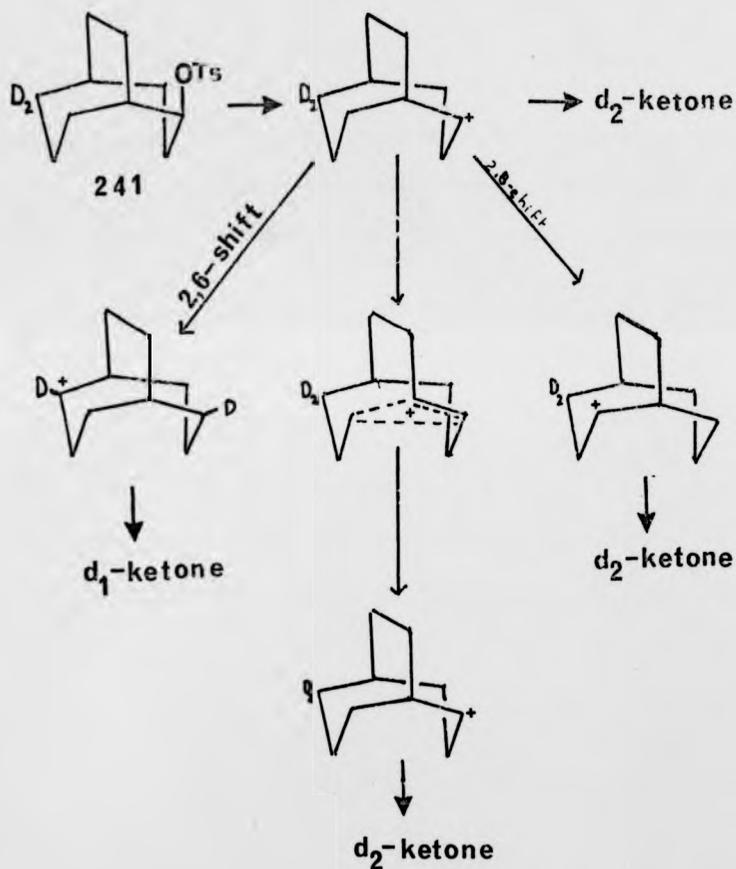
Further, to accommodate the proposed 2,8-shift, it is necessary to assume that all the 2-bicyclo(3.3.1)nonanone formed is from the endo,exo-diol (197), and that the oxygen atom in the ketone group is that from the exo-hydroxyl group, although elsewhere in the same work,

Shaefer shows that exo-2-hydroxyl groups are dehydrated preferentially to endo-2-hydroxyl groups. It is thus unlikely that a 2,8-hydride shift is taking place in the solvolysis of the exo-2-tosylate (204). Because of the non-intermediacy of a non-classical ion in exo-2-bicyclo(3.3.1)nonyl tosylate, the non-classical ion (216) is also perhaps an unlikely or at any rate, an unimportant intermediate in the solvolysis of exo-2-bicyclo(3.3.2)decyl tosylate. Thus it is probable that the deuterium scrambling is due to a 2,6-hydride shift mechanism in the bridged twin-twist-boat ion (218). This mechanism would be expected to give rise to a 50% hydride shift, and so 50% of the original label should be present in the product after exchange. Since the original deuterium content in the labelled alcohol (219) was 90%, the expected percentage of deuterium after exchange is 45%. Further, 5% of the 2-bicyclo(3.3.2)decanone in the final product will come from the endo-2-acetate (209). If we make the reasonable assumption that this is formed from either of the classical ions (214) or (217), there is the reasonable corollary that no hydride shift will have occurred in the endo-2-acetate. Also, if the classical intermediates are long lived enough to react with solvent to give the endo-2-acetate, some of the exo-2-acetate will also have arisen from this source, also without any hydride shift having occurred. In the classical solvolysis of exo-2-bicyclo(3.3.1)nonyl tosylate, the exo:endo ratio for the 2-acetate is 2.1:1. If we assume a similar ratio for the reaction of classical intermediates in the bicyclo(3.3.2)decane case, we estimate that about 10% of the exo-2-bicyclo(3.3.2)decyl acetate will have been formed from

Scheme 7a



Scheme 7b



intermediates in which we estimate that 15% of the product is from the postulated maximum expected deuterium incorporation. This is not so much greater than the 10% expected from the bridged ion (21) to be an extremely

To distinguish between the 2,6-hydride shift and the 2,8-hydride shift, we prepared 2 separate labelled bicyclo(3.3.2)decane derivatives: (3.3.2)decane-6- D_2 and (3.3.2)decane-6- D_4 . In his studies into solvolysis reactions, we prepared the tosylate. Solvolysis of the D_2 tosylate followed by the same reaction as above distinguished between the 2,6-hydride shift and a non-classical 2,8-hydride shift. A d_4 ketone, the hydrolysis product of the solvolysis of 6,6- D_4 bicyclo(3.3.2)decane, is necessary to distinguish between the two solvolysis pathways (see scheme 7b).

bicyclo(3.3.2)decane-6-OTs

In view of the results obtained from the solvolysis of endo-3-bicyclo(3.3.2)decane-6-OTs

ketone



ketone

intermediates in which no hydride shift has taken place. Thus, we estimate that 15% of the 2-bicyclo(3.3.2)decanone will not have arisen from the postulated 2,6-bridged ion (216). This means that the maximum expected deuterium incorporation after wash out is 38%, which is not so much greater than the observed figure of 32%. Thus, though the bridged ion (216) is not a proven intermediate, we have shown it to be an extremely likely one.

To distinguish clearly between the non-classical ion (216), a 2,6-hydride shift and a 2,8-hydride shift requires the solvolysis of 2 separate labelled tosylates. 2,3,3,4,4-Pentadeutero-exo-2-bicyclo(3.3.2)decanol (220) has been prepared by Doyle³⁵ as a by-product during his studies into solvolysis of the deuterated exo-3-bicyclo(3.3.2)decyl tosylate. Solvolysis of the pentadeutero exo-2- tosylate (220a), followed by the same analytical procedure used in this work will distinguish between a hydride shift mechanism (either 2,6- or 2,8-) and a non-classical ion mechanism, the latter ultimately giving rise to a d_4 ketone, the hydride shifts giving rise to a d_5 ketone (see scheme 7a). Solvolysis of 6,6-dideutero-exo-2-bicyclo(3.3.2)decyl tosylate (241) is necessary to distinguish between 2,6- and 2,8-hydride shifts. This solvolysis will furnish no information concerning non-classical ions (see scheme 7b). This tosylate could be obtained from exo-2-hydroxy bicyclo(3.3.2)dec-6-one (242) which is at present being synthesised.

In view of the observed presence of small quantities of exo- and endo-3-bicyclo(3.3.2)decyl acetates among the products, one other

mechanistic possibility that must be considered is that after the 2-bicyclo(3.3.2)decyl cation (214) has undergone 1,2-shift to the 3-cation (42), a 3,7-hydride shift could take place followed by another 1,2-shift to give the rearranged 2-cation (214). This, however, is unlikely in the extreme. Firstly, such a stepwise route cannot account for the observed stereoselectivity; and secondly, no products from a 1,2-hydride shift were observed by Doyle³⁵ in the solvolysis of exo-3-bicyclo(3.3.2)decyl tosylate. Because the 3-bicyclo(3.3.2)decyl cation gives rise to much greater strain relief than does the 2-cation, it is not surprising that there should be a 1,2-shift from position 2 to position 3, but a shift from C3 to C2 is much less feasible energetically. As a result, such a stepwise mechanism was not seriously considered.

Section (ii)

The Authorization of Ezevelo(3.3.2) Section

The Autoxidation of Bicyclo(3.3.2)Decane

Early on in the course of this research, it became apparent that even saturated bicyclo(3.3.2)decanes "go off" quite readily, while unsaturated derivatives are even more prone to this annoying degree of reactivity. For example, a sample of *exo*-2-hydroxybicyclo(3.3.2)dec-6(7)-ene (157) left in a sealed bottle at room temperature for one month decomposed to a viscous oil, while a sample of bicyclo(3.3.2)decane stored at room temperature was, after several months, totally insoluble in pentane, and its infrared spectrum showed strong hydroxyl absorption.

While the allylic autoxidation of unsaturated compounds was not unprecedented, the reactivity of the saturated hydrocarbon was more striking. Even this, however, was not totally unprecedented, as Doyle had earlier noted the extreme ease with which manxane (94) is autoxidized and had started to investigate the possibility of synthesizing bridgehead substituted manxane derivatives by passing air or oxygen into a solution of manxane in pentane.

Schleyer and Bingham have shown that the bridgehead position in bicyclo(3.3.2)decane is solvolytically very reactive, thus the solvolysis rate constant for bridgehead substituted bicyclo(3.3.2)decanes relative to the adamantane bridgehead is 3×10^4 , and relative to the norbornane bridgehead, 10^{14} . Schleyer has also calculated that there should be a decrease in strain energy of 10 kJ mole^{-1} going from bicyclo(3.3.2)decane to the 1-bicyclo(3.3.2)decyl carbonium ion (156).

Since Schleyer had also found that bicyclo(3.3.2)decane was sufficiently reactive to chromic acid oxidation to give both 1-bicyclo(3.3.2)decanol (14) and bicyclo(3.3.2)decan-1,5-diol (29),²⁹ it was apparent that the bridgehead positions in bicyclo(3.3.2)decane are highly reactive. Accordingly, it was felt to be of mechanistic interest to attempt to substitute the bridgehead positions by oxidation with gaseous oxygen. Also, the reported yields of 1-bicyclo(3.3.2)decanol by chromic acid oxidation was only about 50., and it was hoped that autoxidation of bicyclo(3.3.2)decane might prove a more suitable synthesis of the bridgehead alcohol (14).

The first attempt at direct autoxidation of bicyclo(3.3.2)decane was carried out by passing oxygen through a refluxing solution of bicyclo(3.3.2)decane in pentane, from which all peroxides had been previously removed by passing down a column of basic alumina. The reaction was carried out for 16 hours, then the product was treated with lithium aluminium hydride to reduce peroxides and hydroperoxides to alcohols. The product from this reaction was examined by G.C. which showed a trace quantity of the bridgehead alcohol to be present, but that at least 99% of the reaction product was bicyclo(3.3.2)decane. This result, while disheartening from a preparative point of view, at least showed that we were on the right track. Nonetheless, for the reaction to become preparatively useful it appeared that catalysis was necessary.

Cobalt acetate bromide is reported to be a very active catalyst

for the autoxidation of activated methyl and methylene groups,
particularly benzylic groups. ¹⁶¹ Although our system uses a methine
group, we decided to try this catalyst. A solution of bicyclo(3.3.2)
decane and cobalt acetate bromide in glacial acetic acid was refluxed
overnight while passing in oxygen. GC analysis of the product
showed the presence of both 1-bicyclo(3.3.2)decanol and 1-bicyclo(3.3.2)
decyl acetate. After treatment with lithium aluminum hydride as
before, GC analysis showed about 7% 1-bicyclo(3.3.2)decanol and over
90% unreacted bicyclo(3.3.2)decane.

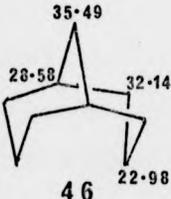
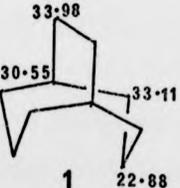
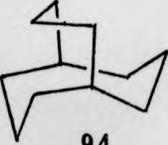
It was thus clear that in principle, autoxidation of bicyclo
(3.3.2)decane to 1-bicyclo(3.3.2)decanol is quite possible, but it is
a slow process, and for it to be preparatively useful would require
much more forcing conditions. It would be of interest to carry out the
reaction in an autoclave at 120°, under a pressure of oxygen with a
cobalt catalyst, such as cobalt naphthenate or perhaps cobalt acetate
bromide.

The decreased reactivity of bicyclo(3.3.2)decane ⁹³⁻¹⁰⁰ compared with
its homologue, manxane (94), ^{35,112} is striking. If a pentane solution
of manxane (94) is stirred under an oxygen atmosphere at room temperature,
a solid hydroperoxide starts to precipitate after an hour or so. This
is found to be a mixture of the mono- and di-hydroperoxides (235 &
236).

The proton decoupled, natural abundance NMR spectra of bicyclo
(2.2.2)octane (191), ⁴⁵ bicyclo(3.3.1)nonane, ¹⁷⁸ bicyclo(3.3.2)decane and

Table 1

^{13}C NMR chemical shift data (δ) and computer calculated hydrocarbon - carborium ion strain energy differences (kJ mole^{-1}).

	$\delta_{\text{C}_1} - \delta_{\text{C}_2}$	ΔH
 191	-83 Hz. ⁴⁵	68.5 ⁴⁶
 46	-78.5 Hz. ¹⁷⁸	35 ⁴⁶
 1	-58.6 Hz.	-10 ⁴⁶
 94	+227 Hz. ⁴⁵	-19 ¹⁷⁹

75
 maximum are of in
 Table 1. It is c
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 the difference bet
 proportion to the
 in the uncalculated
 itself and the bri
 here the difference
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 hydrocarbons. Le
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 in bicyclo(3.3.2)
 considerably less
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 have been no repo
 bicyclo(3.3.1)non
 observation of a
 solvolysis of exo
 analogue process
 Thus we see
 markedly more reac
 nonane, but very
 be of interest to

calculated
differences (kJ mole⁻¹).

ΔH

68.5⁴⁶

35⁴⁶

-10⁴⁶

-19¹⁷⁹

⁴⁵
norbornane are of interest in this respect. The relevant data are in Table 1. It is clear that there is a steady trend for the bridgehead positions to resonate at lower field as the ring size increases, but the difference between bicyclo(3.3.2)decane and norbornane is out of all proportion to the other differences. There is the same observed trend in the calculated strain energy differences between the hydrocarbon itself and the bridgehead carbonium ion ^{46,179} (see Table 1), though here the difference between bicyclo(3.3.2)decane and norbornane is less striking. It is nonetheless clear that the bridgehead position in norbornane is somewhat different to the bridgehead position in other hydrocarbons. Leonard⁴⁵ is of the opinion that the low field position of the bridgehead carbon atoms in norbornane spectra is evidence of bridgehead flattening and increased p-character in the bridgehead carbon hydrogen bond. It is thus not surprising that the bridgehead positions in bicyclo(3.3.2)decane should be unexpectedly reactive, but still considerably less reactive than those in norbornane. Thus, while the bridgehead positions in bicyclo(3.3.2)decane are open to autoxidation, there have been no reports of autoxidation of the bridgehead positions in the bicyclo(3.3.1)nonane ring. Related to this is the already mentioned observation of a 1,2-hydride shift to the bridgehead position in the solvolysis of *exo*-2-bicyclo(3.3.2)decyl tosylate (section (i)). No analogous process occurs in the bicyclo(3.3.1)nonane series.

Thus we see that the bridgeheads in bicyclo(3.3.2)decane are markedly more reactive to autoxidation than those in bicyclo(3.3.1)nonane, but very much less reactive than those in norbornane. It would be of interest to examine a series of flexible bi- and tri-cyclic

hydrocarbons to try and find a reactivity order among them, and find, in particular, a bridgehead position intermediate in reactivity to that in norbornane and that in bicyclo(3.3.2)decane. A very interesting compound in this respect would be the recently synthesised bicyclo¹⁸⁰(5.3.1.1^{3,9})dodecane (192).

Section (iii)

The Reactivity of 9-Bicyclo(3.3.2)nonane

The Reactivity of 9-Bicyclo(3.3.2)Decanone

During the course of the synthetic work described earlier, we were surprised to observe a singular lack of reactivity on the part of 9-bicyclo(3.3.2)decanone (75), and these initial observations have been confirmed by the problems encountered in this ⁹⁸ and other research groups ⁴⁵ when attempting the ring expansion of 9-keto bicyclo(3.3.2)decane derivatives to bicyclo(3.3.3)undecane (94) ^{99, 100, 45} (nonane) derivatives.

A second synthetic result that was initially very surprising was that whereas 9-bicyclo(3.3.1)nonanone (33) reacts cleanly with in situ diazomethane to give only 9-bicyclo(3.3.2)decanone (75); the reaction of bicyclo(3.3.1)non-2-ene-9-one (26) under identical conditions furnished a mixture of 9-epoxyethylene bicyclo(3.3.1)non-2-ene (79) and the ring expansion product, bicyclo(3.3.2)dec-2(3)-ene-9-one (31, 32). On reflection, it appeared that the questions raised by these observations were in fact closely related, the results being explicable in terms of strain in the transition states for the various reactions.

The initial observations of the low reactivity of 9-bicyclo(3.3.2)decanone was in the course of attempts to synthesise 9-bicyclo(3.3.2)decanol (24). Reduction of the ketone with sodium borohydride in methanol, the method usually favoured for such conversions, gave only a 20% yield of the desired alcohol and a 65% yield of a non-

volatile material. Catalytic reduction failed completely, even in glacial acetic acid solution, using a perchloric acid promoted rhodium catalyst.

101
36

Since Wells was unable to reduce selectively the olefinic double bond in bicyclo(3.3.1)non-2-ene-9-one (25), it is apparent that 9-bicyclo(3.3.2)decanone is very markedly less reactive than 9-bicyclo(3.3.1)nonanone (36). This discrepancy was also noted by Leonard in the course of his synthesis of manurene(94) when he found that 9-bicyclo(3.3.2)decanone, itself formed from 9-bicyclo(3.3.1)nonanone by reaction with diazomethane, would not react with diazomethane under any circumstances.

44

The most likely explanation for these phenomena is furnished by Brown's I-strain theory. I-strain is defined initially as "that change in internal strain of a ring compound which results from a change in the coordination number of a ring atom involved in the reaction." The internal strain in any compound is made up of angle, torsional and transannular strain components. The theory predicts a low reactivity for highly strained compounds in reactions involving the making of bonds to one or more of the ring atoms, and a high reactivity in reactions involving bond breaking. Much of the initial work to substantiate the theory was on the acetoxylation of cyclo-allyltosylates, predicted to be fast for highly strained species; and the borohydride reduction of cycloalkanones, predicted

102

4

6

to be slow for the same species. The predictions were born out over a large range of monocyclic systems.

What evidence is there, then, that strain is a significant factor in these reactions? A linear correlation has been observed between the frequency of the $\nu(\text{C}=\text{O})$ band in the infra-red spectrum and the $\text{C}-\widehat{\text{C}}-\text{C}$ bond angle; and Brauman and Laurie^{103, 104} have developed an equation relating carbonyl stretching frequency with the carbonyl bond angle. The observed carbonyl stretching frequency of 9-bicyclo(3.3.2)decanone is 1697 cm.^{-1} , which, using Brauman and Laurie's equation

$$\nu = -2.4\theta + 2006$$

gives a bond angle θ of about 127° . There is thus considerable angle strain in the molecule. By contrast, 9-bicyclo(3.3.1)nonanone has a carbonyl stretching frequency of 1720 cm.^{-1} which corresponds exactly to an unstrained bond angle of 120° . Thus it would appear that while there is strain in the bicyclo(3.3.1)nonane ring, the 9-position is largely unaffected and thus 9-bicyclo(3.3.1)nonanone is of similar reactivity to cyclohexanone.

Of course, the angle strain evidenced by the carbonyl stretching frequency of 9-bicyclo(3.3.2)decanone is unlikely to be sufficient in itself to account for the reduced reactivity; but as the angle strain will be accompanied by transannular and torsional strains, the carbonyl stretching frequency is likely to be a very useful guide to

the overall strain in the molecule. Indeed, Foote¹ has noted a linear relationship between the carbonyl stretching frequency of ketones and the logarithm of the rate constant for acetylation of the corresponding tosylate, provided that there is no chimeric assistance to the solvolysis. Since the rate of tosylate solvolysis is affected to a considerable extent by strain factors in the transition state, it is very reasonable to relate the carbonyl stretching frequency of 9-bicyclo(3.3.2)decanone to the observed lack of reactivity being caused by the strain in the various transition states for the reactions studied.

The I-strain theory predicts a reduced reactivity for any reaction in which the overall internal strain is increased. A reduction of 9-bicyclo(3.3.2)decanone which involves a tetrahedral transition state will thus be difficult, as the internal strain will clearly increase in the transition state. Similarly, the tetrahedral intermediate in the reaction of 9-bicyclo(3.3.2)decanone with diazomethane must be so highly strained that no reaction will occur.

If this explanation is correct, we would predict that the insertion of an olefinic double bond into the bicyclo(3.3.2)decane ring, which should reduce the internal strain, will result in increased reactivity of the keto group at position 9. Evidence for reduced strain comes from the carbonyl absorption of bicyclo(3.3.2)dec-2(3)-ene-9-one (31 and 32), which is at 1704 cm.^{-1} , corresponding to a lower degree of

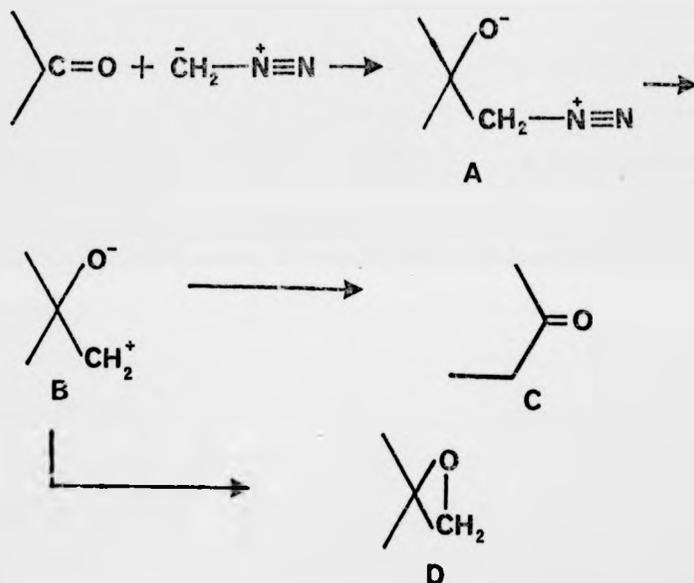
angle strain in the molecule, and, in the light of the previous discussion, it would appear that this molecule is significantly less strained overall.

The reactivity of bicyclo(3.3.2)dec-2(3)-ene-9-one bears out this suggestion - the energy barrier for reactions which involve the conversion of the carbonyl group to a tetrahedral configuration appears to be lower for this unsaturated ketone. Leonard's successful synthesis of manzane included conversion of 9-ketobicyclo(3.3.2)decane derivatives to 9-epoxymethylene bicyclo(3.3.2)decane compounds (95). For bicyclo(3.3.2)dec-2(3)-ene-9-one this conversion could be carried out in a single step using sulphur ylides,^{107,108} but for the saturated 9-bicyclo(3.3.2)decanone the conversion could only be achieved by an indirect route, viz. the epoxidation of 9-oxomethylene bicyclo(3.3.2)decane (96), prepared from the ketone by a Wittig¹⁰⁹ reaction.

Witt has also successfully ring expanded both 9-bicyclo(3.3.2)decanone and bicyclo(3.3.2)dec-2(3)-ene-9-one, using trimethylsilyl cyanide¹¹⁰ to give the trimethylsilyl cyanohydrins (97 and 98), which are reduced with lithium aluminium hydride to the corresponding hydroxylamines (99 and 100) which undergo Tiffen u-Bonjanov ring expansion.¹¹¹ Witt has found that both these bicyclo(3.3.2)decanones react slowly with trimethylsilyl cyanide, compared with the normal¹¹¹ ring and open chain ketones studied by Evans et. al. Thus, while

Scheme 1

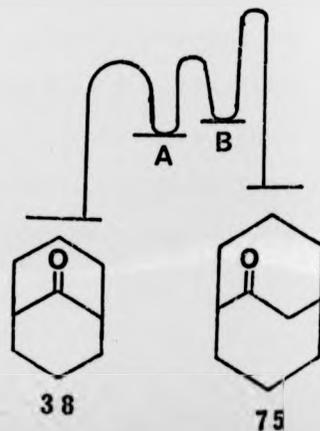
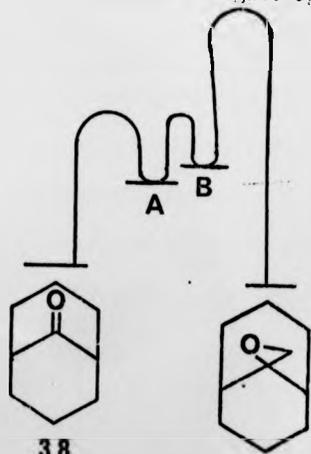
Reaction of ketones with diazomethane.



Schematic energy profile for reaction of 9-bicyclo[3.3.1]nonanone with diazomethane.

Reaction to give epoxide.

Reaction to give ring expansion.



cyclohexanone is
with trialkylsilyl
bicyclo(3.3.2)dec-
hours to go to con
similar conditions

It is apparent
a markedly unreact
lesioned product
where in the bicyc
ketones is readily

Turning now to
and unsaturated 9-
that the 1-strain
epoxide formation
diazomethane.

The first step
the formation of a
undergo ring closure
structure, or by ri
trigonal structure
formation is always
any given situation
barriers separating
C and D.

cyclohexanone is reported to react rapidly at room temperature with trimethylsilyl cyanide, in the presence of zinc iodide, bicyclo(3.3.2)dec-2(3)-one-9-one requires refluxing at 110° for 24 hours to go to completion, and 9-bicyclo(3.3.2)decanone under similar conditions, has reacted only to the extent of about 50%.¹¹²

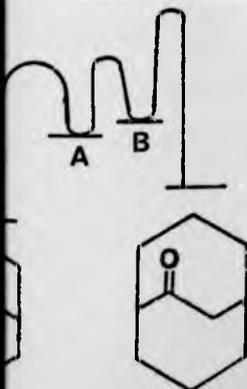
It is apparent, then, that in 9-bicyclo(3.3.2)decanone we have a markedly unreactive ketone; further, that this unreactivity is lessened somewhat by the insertion of an olefinic double bond elsewhere in the bicyclo(3.3.2)decane ring. The reactivity of these ketones is readily explained in terms of the I-strain theory.

Turning now to the related question of the reactions of saturated and unsaturated 9-ketobicyclo(3.3.1)nonanes with diazomethane, we see that the I-strain theory can also account for the observed absence of epoxide formation in the reaction of 9-bicyclo(3.3.1)nonanone with diazomethane.

The first step of the reaction of diazomethane with a ketone is the formation of a tetrahedral intermediate, which can then either undergo ring closure to an epoxide, thus preserving the tetrahedral structure, or by ring expansion, thus returning to the original trigonal structure (see scheme 1). Thus the potential for epoxide formation is always present, and the amount of epoxide formation in any given situation must depend on the relative heights of the energy barriers separating the intermediate B in scheme 1 from the products C and D.

9-bicyclo[3.3.1]

reaction to give
ring expansion.



From the earlier discussion, one might predict that 9-bicyclo (3.3.2)decanone would be more strained than 9-epoxycyclohexene bicyclo(3.3.1)nonane, since 9-bicyclo(3.3.1)nonanone is easily converted to tetrahedral structures, for example by catalytic reduction or by cyanohydrin formation. Thus one might be tempted to predict that reaction of 9-bicyclo(3.3.1)nonanone with diazomethane should give mainly the epoxide. However, this line of thought does not consider the relative energies of the intermediate transition states. It is quite conceivable that the transition state for the closure of B to an epoxide D be of higher energy than that for ring expansion to C, for this particular reaction. Certainly, it is reasonable in terms of the I-strain theory that a transition state leading to a tetrahedral product should be more strained than that leading to a trigonal product.

This explanation is supported by the observation of the formation of considerable quantities of epoxide in the reaction of bicyclo (3.3.1)non-2-ene-9-one with diazomethane. Here again, the insertion of the olefinic double bond will reduce the overall internal strain in the molecule; thus the increase in strain going to the transition state for epoxide formation and that going to the transition state for ring expansion should be more nearly alike.

Indeed, it appears that the ratio of epoxide to ring expanded product in this reaction is extremely sensitive to reaction conditions. Thus, while the ratio observed in this work has always been of the

order of 50:50, Leonard reports that under strongly basic conditions,
no epoxide is formed. ⁴⁵ However, a single attempt in these laboratories
to duplicate this reaction was found to be physically impossible;
the assumption of a misprint in Leonard's paper led to conditions
which gave rise to epoxide only! ¹¹²

We have seen that the reactions of 9-bicyclo(3.3.1)non-2-ene-
9-one with in situ diazomethane are explicable in terms of the I-
strain theory. Similarly, the initially surprising lack of reactivity
of 9-bicyclo(3.3.2)decanone is also completely accounted for by this
concept. Although only a comparatively small piece of work, these
results are nonetheless a useful addition to the evidence in favour
of this theory.

Section (iv)

The Synthesis of Bicyclo(3.3.2)deca-2,6-diene

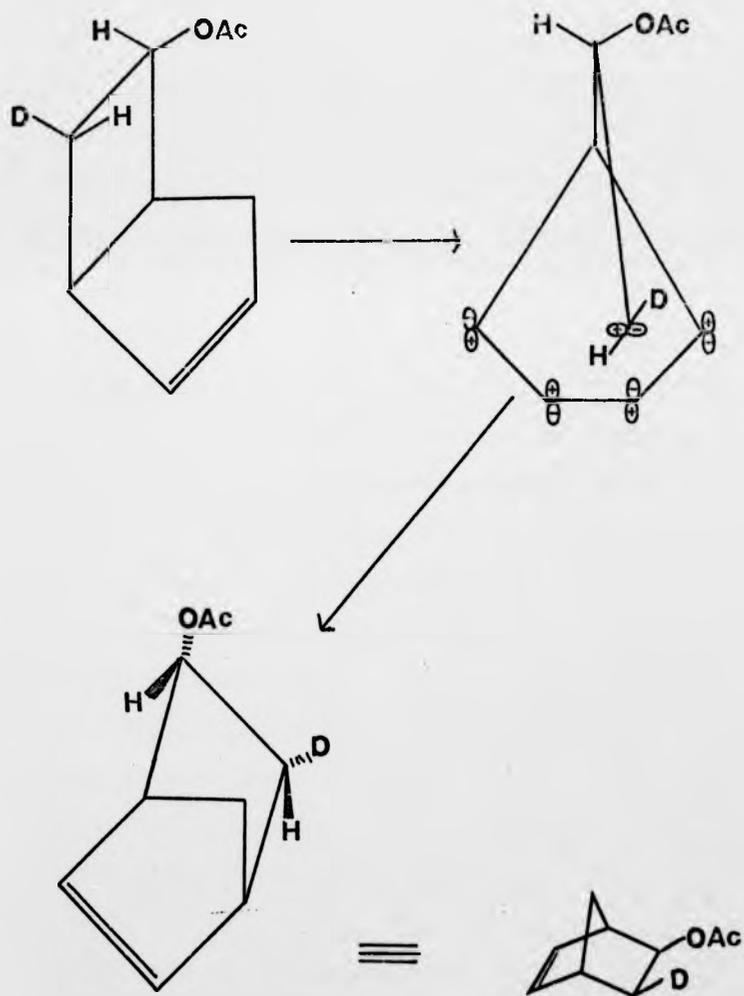
The Synthesis of Mirclo(3,1,2)Dec-2,6-Diene.

Woodward and Hoffman define a sigmatropic change of order (i,j) as "the migration of a σ -bond, flanked by one or more π -electron systems, to a new position whose termini are i-1 and j-1 atoms removed from the original bonded loci, in an uncatalyzed, intramolecular process." ¹⁶⁷ as examples they cite the well known Cope and Claisen rearrangements as (3,3) sigmatropic rearrangements. In principle, such rearrangements can occur by two stereochemically different routes. In a suprafacial process, the migrating group is associated at all times with the same face of the π -system, while in an antarafacial process, the migrating group is passed from the upper face of the carbon atom from which migration is occurring, to the lower face of the carbon atom to which it is migrating.

From orbital symmetry considerations it is possible to predict the possible reaction pathways for any given situation. At the same time it is necessary to note that in certain situations theoretically allowed processes may not be able to occur for steric reasons - for example, antarafacial processes are not possible within small and medium sized ring systems; while in any system, a process that would require such distortion of the carbon framework as to seriously impair π -electron delocalisation will also not occur.

The simple treatment outlined briefly above makes the prediction that a (1,3) sigmatropic rearrangement, in which a σ -orbital of the

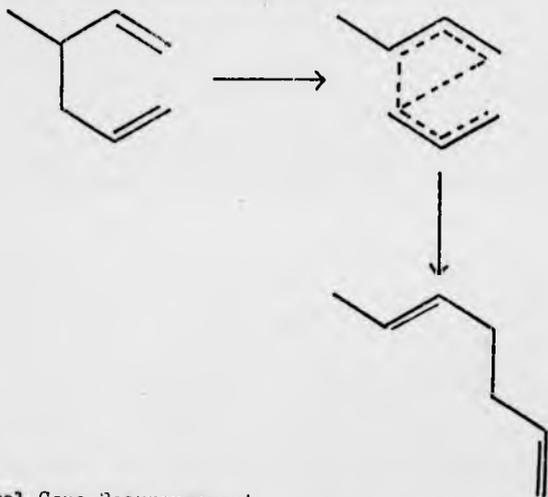
Scheme 1



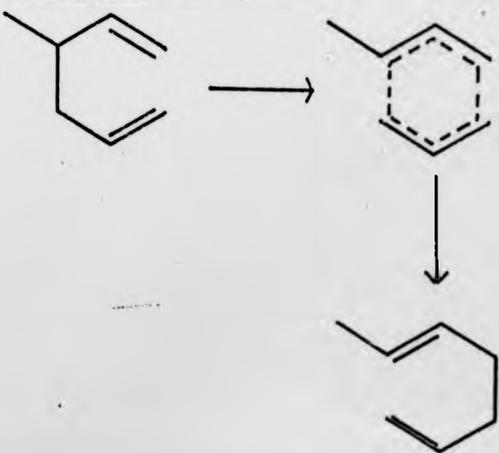
after Berson^{168, 169}.

Fig 1

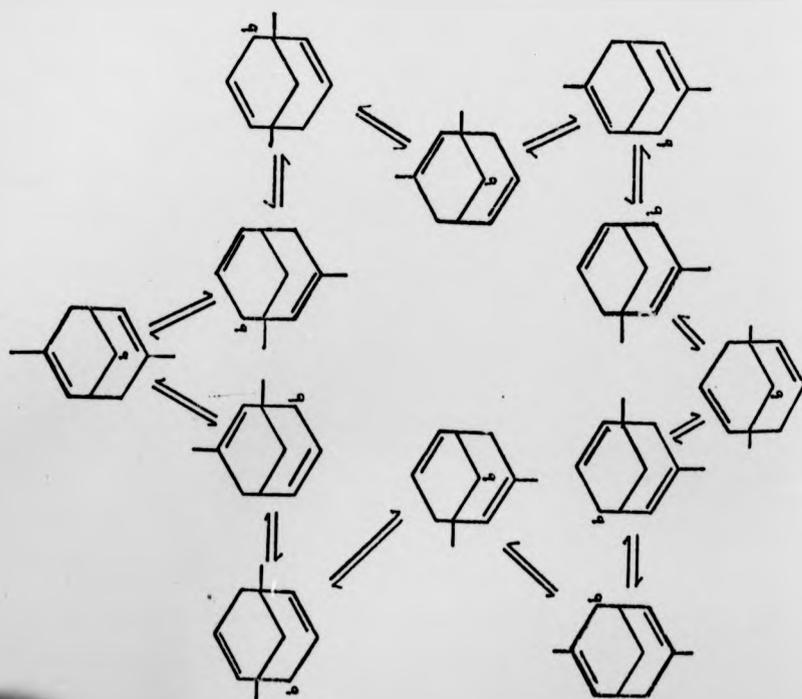
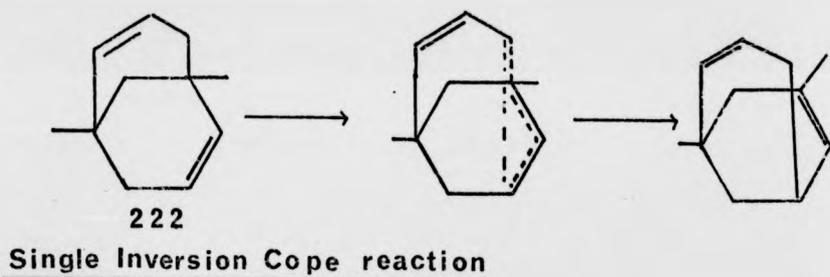
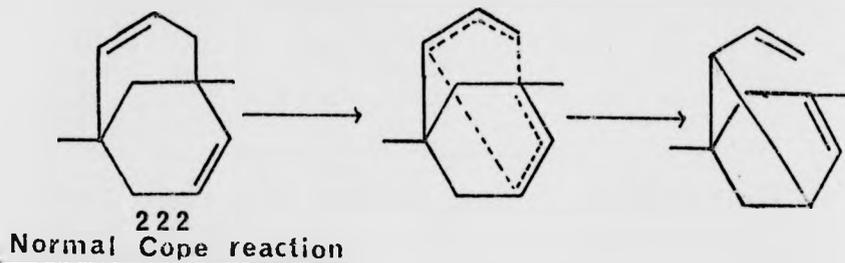
Single Inversion Cope Rearrangement.



Normal Cope Rearrangement

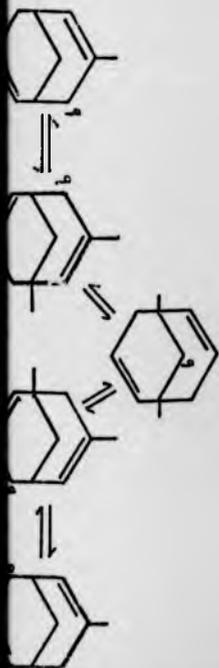
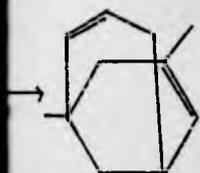
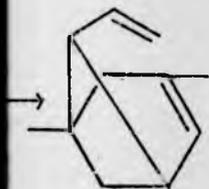


Scheme 2



unreacting group is
antarafacial rather
sterically imposed
low lying π -orbitals
provided that the
Person and his co-
in fact occur during
3-enyl acetate (22)
through the 4-orbitals
to examine the nature
that would be gener
(See Fig. 1). This
51,170
ment". This is

rearrangement is pr
A suitable net
would be to choose
while the normal Co
strained transition
diene (43). In this
degenerate, but it
tation of the bridge
Single Inversion Co
non-2,5-diene (222)
The early stud
diene (43) were car



migrating group is interacting with the π -system, must occur by an antarafacial pathway, and, as already stated, such a process is sterically impossible within small and medium rings. However, if a low lying π -orbital is available, a suprafacial process is allowed, provided that the migrating group can invert its configuration.

Person and his co-workers^{133,169} have shown that such an inversion does in fact occur during the thermolysis of syn, cis-4-bicyclo(3.2.0)hept-3-enyl acetate (221). (See scheme 1). This rearrangement proceeds through the 4-orbital transition state shown, and it would be interesting to examine the nature of the corresponding 6-orbital transition state that would be generated when the migrating group is an allyl system. (See Fig. 1). This is the so-called "Single Inversion Cope Rearrangement"^{51,170}. This is difficult to detect unless the normal Cope rearrangement is prevented. (Fig. 1).

A suitable method of studying the Single Inversion Cope Rearrangement would be to choose a system in which this reaction can occur easily, while the normal Cope Rearrangement is inhibited because it has a more strained transition state. Such a system is bicyclo(3.3.1)nona-2,6-diene (43). In this case, the Single Inversion Cope Rearrangement is degenerate, but it could be detected by deuterium labelling or substitution of the bridgehead positions by methyl groups. The normal and Single Inversion Cope Rearrangements of 1,5-dimethylbicyclo(3.3.1)nona-2,6-diene (222) are shown in scheme 2.

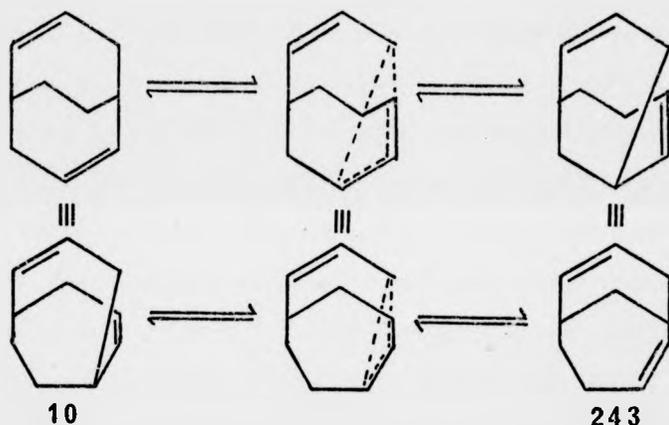
The early studies of thermal reactions of bicyclo(3.3.1)nona-2,6-diene (43) were carried out by Bishop, who showed that on heating at

300°, (this is the temperature used by Benson in his studies) bicyclo-
(3.3.1)nona-2,6-diene³¹ was recovered unchanged. This indicates that
no normal Cope rearrangement is occurring at this temperature, as
expected, but of course yielded no information as to whether the single
inversion process was in fact taking place.

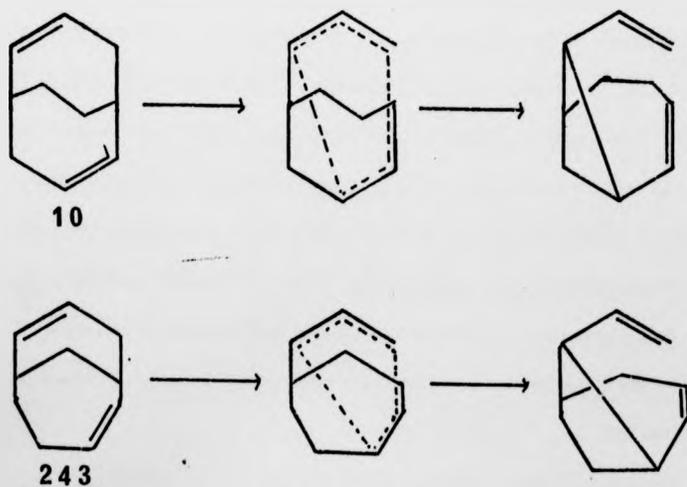
The labelling schemes chosen by Parker and Bishop were a) the
synthesis of 3,7-dideuterobicyclo(3.3.1)nona-2,6-diene (223) and b)
the synthesis of 1,5-dimethylbicyclo(3.3.1)nona-2,6-diene (222). Both
these syntheses have proved more problematical than expected. The
original synthesis of bicyclo(3.3.1)nona-2,6-diene¹⁷¹ involved dehydro-
halogenation of 2,6-dibromobicyclo(3.3.1)nonane (224) in a sealed tube
at 245° with dicyclohexylethylamine. At this temperature, it is likely
that the Single Inversion Cope Rearrangement will take place, and so
scramble the label. Hence a new, low temperature synthesis, in which
there is no danger of scrambling, nor of any deuterium label being
exchanged had to be designed. So far this has not been entirely
successful. Some partially deuterated bicyclo(3.3.1)nona-2,6-diene
has been obtained by Bishop, but since the detection of the rearrangement
using deuterium labelling is dependant on careful integration of NMR
signals, a deuterium content of as near to 2 deuterium atoms per
molecule as possible is necessary. For the methyl labelling experiment,
Bishop has prepared 1,5-dimethylbicyclo(3.3.1)nona-2,6-diene (225), but
this has not yet been converted to the desired 1,5-dimethylbicyclo(3.3.1)-
2,6-diene.

Scheme 3

Equilibration of bicyclo[3.3.2]deca-2,6-diene and bicyclo[4.3.1]deca-2,7-diene via Single Inversion Cope Rearrangement.



Normal Cope Rearrangements of bicyclo[3.3.2]deca-2,6-diene and bicyclo[4.3.1]deca-2,7-diene.



If bicyclo(3.3.2) Inversion Cope ~~and~~ deca-2,6-diene (10) bicyclo(3.3.2) ~~and~~ (4.3.1)deca-2,7-diene to bicyclo(3.3.2) ~~and~~ dienes should lead also, in principle Bishop's observation these rearrangements are

The only reference literature is as a of bullvalene; the material was not e

As noted in the bicyclo(3.3.2)deca dibromobicyclo(3.3.2) bullvalene with bromo bullvalene dibromide from which the room temperature dehydro present non-availa bullvalene rule of A suitable pr

e and bicyclo[4.3.1]

arrangement.



III



243

deca-2,6-diene



If bicyclo(3.3.1)nona-2,6-diene (43) does undergo the Single Inversion Cope rearrangement, it is highly probable that bicyclo(3.3.2)deca-2,6-diene (10) will do so as well. Further, the rearrangement of bicyclo(3.3.2)deca-2,6-diene is not degenerate; the product is bicyclo(4.3.1)deca-2,7-diene, (243) which can itself undergo rearrangement back to bicyclo(3.3.2)deca-2,6-diene (10). Thus pyrolysis of either of these dienes should lead to the same equilibrium mixture. Both dienes can also, in principle, undergo normal Cope rearrangements, but in view of Bishop's observations on bicyclo(3.3.1)nona-2,6-diene, it is likely that these rearrangements will also be strongly inhibited. (All these rearrangements are shown in scheme 3).

The only reference to bicyclo(3.3.2)deca-2,6-diene (10) in the literature is as a by-product from the sodium/liquid ammonia reduction of bullvalene; the structure was not proven, only suggested, and the material was not characterized.

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As noted in the introduction, probably the best synthesis of bicyclo(3.3.2)deca-2,6-diene would be from bullvalene dibromide, 4,8-dibromobicyclo(3.3.2)deca-2,6,9-triene (14), made by treatment of bullvalene with bromine in methylene chloride. Catalytic reduction of bullvalene dibromide will give 2,6-dibromobicyclo(3.3.2)decane (226) from which the required diene (10) should be obtainable by a low temperature dehydrohalogenation in acceptable yield. However, the present non-availability of cyclo-octatetraene from which to prepare bullvalene ruled out this synthesis.

A suitable precursor for this synthesis (and much other work in

the bicyclo(3.3.2)decane series) would be 1,3,5,7-tetracarboxymethoxy bicyclo(3.3.2)deca-2,6-dione (227); the homologue of Meerwein's ester (228). In view of the potential value of this compound, a single attempt was made to condense two moles of dimethyl methylene malonate with one mole of 1,1,4,4-tetracarboxymethylbutane in the presence of sodium methoxide, as for Meerwein's ester. Not totally unexpectedly, several acidic products were obtained, all considerably more acidic than Meerwein's ester; and this admittedly fanciful synthesis was abandoned.

A more promising route to the diene became available from the product of trifluoroacetylolysis of exo-2,3-epoxybicyclo(3.3.2)decane, viz. exo-2-hydroxybicyclo(3.3.2)dec-6(7)-ene (167) of which about 70% was known to have the desired 2,6-substitution pattern (see section (i) for full details).

Formation of the corresponding tosylate, followed by treatment with potassium tert.-butoxide in dimethyl sulphoxide at 60° gave an oil, which on GLC analysis (S.T.O.P. Carbowax 20M) showed three peaks in the ratio 16:28:56. The infra red spectrum showed strong carbon-oxygen stretching bands, so it was probable that the major (56%) component (also the most polar) was 2-bicyclo(3.3.2)dec-6(7)-enyl tert.-butyl ether (229), while presumably the other two components were bicyclo(3.3.2)deca-2,6-diene (10) and bicyclo(3.3.2)deca-2,7-diene (230). However, these two less polar components were not easily separated to check their identity. The formation of over 50% tert.-butyl ether is

rather surprising, particularly in a system where the formation of sp^2 centres is generally favoured. It is perhaps possible that since there is already one double bond in the system, inclusion of a second might increase the overall ring strain, and thus substitution would be favoured.

After other reaction sequences resulting in even less success, bicyclo(3.3.2)deca-2,6-diene was finally prepared, albeit in very poor yield, by dehydration of exo-2-hydroxybicyclo(3.3.2)dec-4(7)-ene (167) with thionyl chloride in pyridine solution at 40° . The reaction product contained many materials, but one (the least polar) was shown by GLC to be identical with the 26% component from the tosylate elimination reaction, tentatively assumed to be the desired bicyclo(3.3.2)deca-2,6-diene. This was the only olefinic product from the dehydration reaction, and was present to the extent of only 20%. Apparently, therefore, exo-2-hydroxybicyclo(3.3.2)dec-7-ene (168) is not dehydrated by thionyl chloride:pyridine.

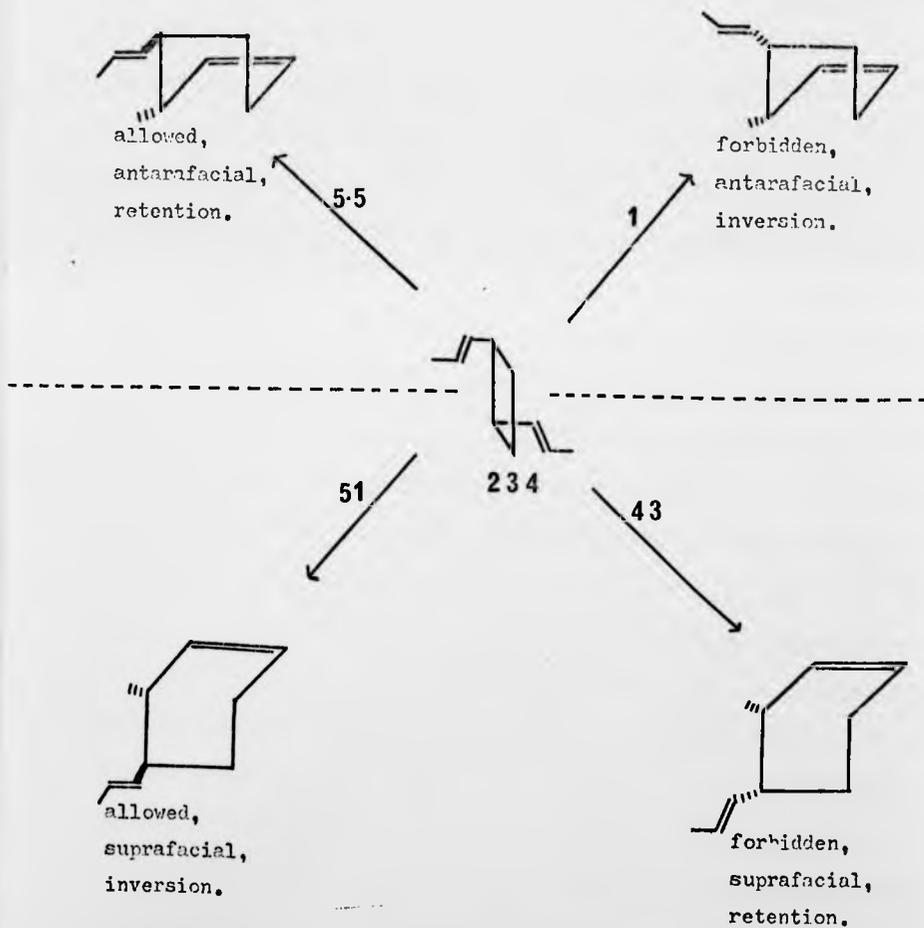
The original tentative assignment of the 16% component of the tosylate elimination reaction as bicyclo(3.3.2)deca-2,7-diene was strengthened by its being shown not to be any of bicyclo(3.3.2)decane, 2-bicyclo(3.3.2)decene or 9-bicyclo(3.3.2)decene, by GLC comparison.

The olefinic product from the dehydration reaction was readily separated from the other components of the product mixture by preparative GLC, which furnished a small quantity of a white solid. All the spectral data were consistent with its being the desired bicyclo(3.3.2)deca-2,6-diene, but the isomeric bicyclo(3.3.2)deca-2,7-diene could not

he ruled out, even using 220MHz. ¹⁷⁴ Fortunately, we were able to obtain copies of the NMR spectra of bicyclo(3.3.1)nona-2,6-diene and bicyclo(3.3.1)nona-2,7-diene (232) ¹⁷⁵ from Professor Hans Huiso (Organisch-Chemisches Institut, Universität Karlsruhe, Germany); and comparison of these spectra, and that of bicyclo(3.3.0)octa-2,6-diene (231) ¹⁷⁶ with the spectra of the bicyclo(3.3.2)deca-diene showed that our diene was the expected and desired 2,6-isomer. The conclusive evidence came from the olefinic proton signals. In all the cases examined, the resonance was complex, but for both the known $\Delta^{2,6}$ dienes (23 & 231) the band width of the olefinic signals was 30Hz., while that for the $\Delta^{2,7}$ diene (232) was 50Hz. Since the olefinic resonance of the unknown bicyclo(3.3.2)deca-diene also had a band width of 30Hz., and a very similar splitting pattern to that of bicyclo(3.3.1)nona-2,6-diene in particular, it seemed very reasonable to assign the bicyclo(3.3.2)deca-diene as the required $\Delta^{2,6}$ isomer (10), particularly as it is also the major diene from the tosylate elimination reaction. However, the overall yield of less than 5% after purification is hardly satisfactory, and because of the small quantity of material and its extreme instability to air (bicyclo(3.3.2)deca-2,6-diene displays a pronounced tendency to autoxidise), it has so far proved impossible to perform any experiments to see if a Single Inversion Cope Rearrangement does in fact take place.

Two other pieces of work merit reference in this context. Firstly, Baldwin ¹⁷⁵ has made a pyrolytic study of bicyclo(3.3.0)octa-1,6-diene (231). However, he was looking for a degenerate rearrangement process, rather than a Single Inversion Cope Rearrangement, which would give

Fig 2



The dotted line divides optical isomers.

Figures refer to relative rates of product formation.

After Berson and Dervan¹⁷⁷.

bicyclo(3.2.1)octa-2,5-diene would be expected to undergo electrocyclic ring closure to form bicyclo(3.2.1)octane. The structure of this bicyclo(3.2.1)octane is shown below. The structure of this bicyclo(3.2.1)octane is shown below.

Secondly, the electrocyclic ring closure of bicyclo(3.2.1)octa-2,5-diene to form bicyclo(3.2.1)octane is a suprafacial process. The structure of this bicyclo(3.2.1)octane is shown below.

to detect the relative rates of formation of the two products. The relative rates of formation of the two products are shown in the figure. The relative rates of formation of the two products are shown in the figure.

Berson finds that the electrocyclic ring closure of bicyclo(3.2.1)octa-2,5-diene to form bicyclo(3.2.1)octane is a suprafacial process. The structure of this bicyclo(3.2.1)octane is shown below.



Forbidden,
antarafacial,
inversion.



Forbidden,
suprafacial,
retention.

bicyclo(3.2.1)octa-2,6-diene (213). The degenerate rearrangement did not take place, but at 450° several other olefinic products were found to be formed, but these were not investigated. One of these might well be the bicyclo(3.2.1)octa-2,6-diene expected from the Single Inversion Cope rearrangement. The rearrangement of bicyclo(3.3.2)nona-2,6-diene would be expected to be quite difficult, because the near planar structure of this diene means that the π -orbitals cannot approach as closely as in a more flexible system such as bicyclo(3.3.2)nona-2,6-diene or bicyclo(3.3.1)nona-2,6-diene.

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Secondly, some very elegant work by Berson¹ on the thermal, sigmatropic rearrangement of trans-1,2-trans,trans-dipropenylcyclobutane (234), also a big-allyl system like the potential rearranging system in bicyclo(3.3.2)nona-2,6-diene, has very recently appeared in the literature. By using an optically active substrate, Berson was able to detect the relative amounts of the four possible products that could arise (see Fig. 2). It is found that 1,3-suprafacial sigmatropic shift, with inversion (i.e. a single inversion Cope rearrangement, is the most favoured pathway, but it is only slightly favoured over the forbidden analogous rearrangement with retention of configuration. Antarafacial rearrangements are not favoured.

Berson feels that the results could be explained by a diradical intermediate, but he prefers to explain these results as concerted sigmatropic rearrangements, with a very low energy barrier between the allowed and forbidden processes.

EXPERIMENTAL

"If Mr. Jennings will permit me," pursued the old lady, "I should like to ask a favour. Mr. Jennings is about to try a scientific experiment to-night. I used to attend scientific experiments when I was a girl at school. They invariably ended in an explosion. If Mr. Jennings will be so very kind, I should like to be warned of the explosion this time. With a view to getting it over, if possible, before I go to bed.

"The Moonstone" by Wilkie Collins

General

Melting points were recorded in sealed capillary tubes heated in an aluminium block, and are uncorrected. Mass spectra were determined by the Physico-Chemical Measurements Unit (PCMU) at Aldermaston on an AEL M.S.9 spectrometer. Ultraviolet absorption spectra were recorded in ethanol solution on a Unicam SP800 spectrophotometer. Routine infra-red spectra were determined in carbon tetrachloride solution (unless otherwise stated) on Perkin-Elmer 157G and 457 spectrophotometers. High resolution infra-red spectra were recorded as carbon tetrachloride solutions by Mrs. M. Berry on a Perkin-Elmer 521 spectrophotometer; and by Mrs. F. Lawrie on a Perkin-Elmer 225 spectrophotometer at the University of Glasgow. Routine nuclear magnetic resonance spectra were measured in carbon tetrachloride solution (unless otherwise stated) on a Perkin-Elmer R10 (60MHz.) spectrometer using tetramethylsilane as internal reference. High resolution NMR spectra were recorded by PCMU on Varian Associates HA100 (100MHz.) and HA220 (220MHz.) spectrometers. Fourier transform ^{13}C NMR spectra were determined in deuterio-chloroform solution at Queen Mary College, London, on a Bruker Spectrospin (22.63 MHz) spectrometer, using TMS as internal standard. Microanalyses were carried out at Oxford by Dr. F. B. Strauss and his staff. Thin layer chromatography was carried out on baked Kieselgel G plates, which were developed with iodine vapour. Analytical gas-liquid chromatography was carried out on a Perkin-Elmer F 11 instrument. Preparative gas-liquid chromatography

was performed on a Varian Aerograph 700 instrument. Light petrol refers to the fraction b.p. 40-60°. Organic extracts were dried with magnesium sulphate unless otherwise stated. Alumina for chromatography was Laporte type H, deactivated with 5% w/w water, unless otherwise stated. Silica gel for chromatography was Hopkin and Williams' grade M.F.C.

N.B. All compounds containing the bicyclo(3.3.2)decane ring system were treated as if they were both volatile and unstable in air. They were therefore always stored in sealed containers under a blanket of nitrogen, at -20°C.

9-Bicyclo(3.3.2)decanone

9-Bicyclo(3.3.1)nonanone (40g.), potassium hydroxide (18g.), and water (60ml.) were dissolved in methanol (400ml.). The mixture was cooled in an ice bath, and a solution of α -methyl- β -nitroso-p-toluene-sulphonamide (175g.) in methanol (900ml.) was added slowly with stirring, the reaction temperature being held below 20°. Stirring was continued for a further 15 hours after addition was completed, and the mixture was then concentrated in vacuo, diluted with water (2l.) and extracted three times with ether. Evaporation of the ether yielded an oily residue, a mixture of 9-bicyclo(3.3.2)decanone and methyl tosylate. This residue was dissolved in ethanol (200ml.), and water (150ml.) and sodium hydroxide (10g.) were added. The mixture was boiled under reflux for 15 hours, cooled, diluted with water (500ml.) and extracted with pentane (3x150ml.). The combined pentane extracts were washed with water and dried, the pentane was distilled off and the residue was sublimed to give 9-bicyclo(3.3.2)decanone (29g., 70%), m.p. 180-182°. (The literature gives m.p. 110-115°, ³⁵177-179°, ⁴⁵and ²⁹182-184°).

Semicarbazone: m.p. 223-225°

IR(cm.⁻¹) : 3370, 2925, 2363, 1697, 1485, 1450, 1405, 1379, 1369, 1358, 1349, 1210, 1180, 1106, 1075, 934, 878.

IR(τ) : 7.1 (IR); 7.46 (doublet, J_{AB} = 6Hz., 2H); 7.75 (13H).

¹³C NMR(δ) : 214.55 (39); 51.56 (310); 47.41 (31); 32.42 (34, 36); 28.80 (35); 27.51 (32, 38); 21.90 (33, 37).

Bicyclo(3.3.2)decane

9-Bicyclo(3.3.2)decanone (10g.) and hydrazine hydrate (100%, 4.2ml.) were added to a solution of sodium (3.5g.) in digol (160ml.). The reaction mixture was warmed for 1 hour, and then heated under reflux for a further 3 hours, during which the product sublimed into the condenser. When the reaction mixture had cooled, the product was washed from the condenser with pentane, and the pentane solution was washed with water and dried over basic alumina. Distillation of the pentane yielded bicyclo(3.3.2)decane (6.2g., 56%), m.p. 177-179°. (The literature gives m.p. 177-178°, 179-181°, 164-165°, and 165°²⁴²⁹²¹³⁵). A further quantity of hydrocarbon (1.6g.) was obtained from the cooled reaction mixture, by diluting with water (250ml.) and extraction with pentane (3x50ml.). The pentane extracts were washed twice with water and dried over basic alumina. Distillation of the pentane yielded a waxy solid that was purified by vacuum sublimation, m.p. 175-177°. (total yield: 7.9g., 89%).

IR(cm.⁻¹) : 2990 (sh), 2918, 2865, 1485, 1465, 1450.

NMR(τ) : 7.8 (br., 2H); 8.22, 8.25, 8.28, (4H); 8.35 (12H).

¹³C NMR (δ): 33.98 (C₉, C₁₀), 33.11 (C₂, C₄, C₆, C₈), 30.55 (C₁, C₅), 22.88 (C₃, C₇).

1-Bicyclo(3.3.2)decanol

Chromium trioxide (1.6g.) was added to a stirred solution of bicyclo(3.3.2)decane (1g.) in acetic acid (15ml.) and acetic anhydride (15ml.), in small portions over 1 hour, the temperature being maintained

below 30°. After stirring for a further 45 minutes, the reaction mixture was poured onto ice and extracted with ether (3x50ml.). The combined organic extracts were washed with saturated sodium bicarbonate, and then dried. Lithium aluminium hydride (100mg.) was then added and the mixture was stirred at room temperature for 2 hours. The excess hydride was destroyed by the cautious addition of water, the inorganic salts were filtered off, and the solvent was removed to give a crude product which was adsorbed on alumina from light petrol. Elution with light petrol yielded unreacted bicyclo(3.3.2)decane (50mg.); elution with ether/light petrol (50:50) furnished 1-bicyclo(3.3.2)decanol (450mg., 40%), which was purified by vacuum²⁹ sublimation, m.p. 193-198°. (The literature gives m.p. 191-194°). IR(cm.⁻¹): 3612, 2989 (sh.), 2929, 2870, 1486, 1465, 1454, 1074, 996, 924, 875. $\mu_{max}(\tau)$: 7.61 (sharp, 1H); 7.8 (broad, 1H); 8.32 (16H).

Bicyclo(3.3.2)decane-1,5-diol

Chromium trioxide (2.0g.) was added in small portions to a stirred solution of bicyclo(3.3.2)decane (1g.) in acetic acid (15ml.) and acetic anhydride (15ml.), over 90 minutes, the reaction temperature being maintained below 40°. After stirring at 30° for a further 4½ hours the mixture was poured onto ice, and extracted with methylene chloride (3x50ml.). The combined organic extracts were washed with 2% sodium hydroxide solution (150ml.), saturated aqueous sodium

bicarbonate (30ml.), and dried. The solvent was evaporated, leaving a yellow oil which was dissolved in anhydrous ether, and treated with a slurry of lithium aluminum hydride (100mg.) in ether. The mixture was stirred overnight at room temperature, the excess hydride was destroyed by the cautious addition of water, and the inorganic salts were filtered off and washed with methylene chloride. The combined organic extracts were dried and the solvents were evaporated, leaving a white gum which was recrystallized from light petrol/ether (70:30) to yield bicyclo(3.3.2)decane-1,5-diol (420mg., 34%), m.p. 214-218°. (The literature ²⁹ gives m.p. 214-217°).

Found: C, 70.00; H, 10.75. Calc. for $C_{10}H_{18}O_2$; C, 70.55; H, 10.65%.

IR(KBr) (cm^{-1}): 3250, 2979, 2942, 2920, 2850, 1454, 1464, 1452, 1368, 1232, 1018, 1000.

($CDCl_3$) (cm^{-1}): 3685, 3607, 3450, 2982 (sh.), 2871, 1445, 1355, 1330, 1235, 1060, 1016, 1100.

NMR ($CHCl_3$) (τ): 8.16, 8.21 (16H); 5.40 (2H).

n_D^{20} : 1.470.

1-Chlorobicyclo(3.3.2)decane

1-Bicyclo(3.3.2)decanol (90mg.) was added to redistilled thionyl chloride (1ml.). After standing for 12 hours, chips of ice were added until all thionyl chloride was destroyed. The reaction mixture was then extracted with ether (2x10ml.) and the combined extracts were washed once with water and dried over potassium carbonate. Removal

of the solvent by distillation and sublimation of the residue gave
1-chlorobicyclo(3.3.2)decane (45mg., 41%), m.p. 25-27°. (The
literature¹⁹ gives m.p. 51-57°).

IR (cm.⁻¹): 2933, 2920, 2666, 1464, 1452, 1451, 1356, 1067, 942, 913,
881, 858, 891, 824.

NMR(τ): 7.70 (multiplet, 8H); 8.34 (multiplet, 11H).

1,1-Dichlorobicyclo(3.3.2)decane

Distilled thionyl chloride (5ml.) was added to a stirred solution
of bicyclo(3.3.2)decane-1,5-diol (210mg.) in methylene chloride (20ml.).
The diol was partially reprecipitated, and the mixture was stirred at
room temperature for 20 hours, after which time the solution was clear.
Chips of ice (10g.) were added to destroy excess thionyl chloride, and
the organic layer was separated and dried over potassium carbonate.
The solvent was distilled and the residue was sublimed in vacuo. The
sublimate was crystallized from methanol to give 1,1-dichlorobicyclo
(3.3.2)decane (154mg., 64%), m.p. 34-36°, as white needles.

Found: C, 57.70; H, 7.90; Cl, 33.15. $C_{10}H_{16}Cl_2$ requires C, 57.75;
H, 7.60; Cl, 34.20.

IR (cm.⁻¹): 2982 (sh.), 2950, 2666, 2662, 1485, 1463, 1452, 1365,
922, 864.

NMR(C_6H_6 , τ): 7.91, 7.98, 8.08 (multiplets, 10H); 8.78 (multiplet, 4H).

M^+ : no parent ion. M^+-Cl : m/e 171.

High resolution: m/e 171.0541. $C_{10}H_{16}Cl^+$ requires 171.0941.

Bicyclo(3.3.2)heptan-9,10-dione

A solution of 9-bicyclo(3.3.2)heptanone (1g.), selenium dioxide (1.4g.) and water (1ml.) in dioxane (20ml.) was heated under reflux for 1 hour. The precipitated selenium was filtered from the cooled reaction mixture and the dioxane was evaporated. The gummy residue was washed with pentane (5ml.), the pentane was decanted and the residue was dissolved in cyclohexane. The solution was filtered through celite, washed with saturated sodium thiosulphate solution (2x20ml.) and dried. Distillation of the solvent yielded a bright yellow solid which was sublimed in vacuo to give bicyclo(3.3.2)heptan-9,10-dione (20mg., 73%), m.p. 192-193°.

Found: C, 71.95; H, 6.35. $C_{10}H_{14}O_2$ requires C, 72.25; H, 6.50%.

IR (cm.⁻¹): 3410, 2938, 2962, 1712, 1485, 1471, 1453, 1365, 1354, 1315, 1288, 1202, 1096, 1050, 1030, 919, 896.

NMR(τ): 6.96 (br., 2H); 8.14 (12H).

¹³C NMR(δ): 200.35 (C9, C10); 47.25 (C1, C5), 28.91 (C2, C4, C6, C8), 21.25 (C3, C7).

UV (m μ): $\lambda_{max} = 421$, $\epsilon = 34$.

M⁺: m/e = 166.

7,8,9,10-Tetrahydro-6,10-propano-6H-cyclohepta(b)aminoxaline

A solution of bicyclo(3.3.2)heptan-9,10-dione (320mg.) and resublimed *o*-phenylene diamine (196mg.) in ethanol (10ml.) was refluxed for 1 hour. The ethanol was evaporated to yield a solid which was

recrystallized twice from 100-120° petroleum ether to give 7,8,9,10-tetrahydro-6,10-propano-5H-cyclohepta(b)imidazoline (300mg., 60%), m.p. 124-124.5°.

Found: C, 60.60; H, 7.60; N, 11.70. $C_{16}H_{18}N_2$ requires C, 60.60; H, 7.60; N, 11.75%.

IR(cm^{-1}): 3070, 2865, 1957, 1930, 905, 1850, 1824, 1488, 1471, 1450, 1440, 1359, 1379, 1327, 1137, 1103, 1090, 940, 932, 870, 671, 610, 578.

NMR(τ): 2.60 (decuplet, 4H); 6.34 (2H); 8.05, 8.12, 8.20 (1H); 8.4-8.5 (1H).

M⁺: m/e 238.

9-Bicyclo(3.3.2)decanol

To a suspension of lithium aluminium hydride (300mg.) in anhydrous ether (10ml.) was added over 15 minutes a solution of 9-bicyclo(3.3.2)decanone (3.6g.) in ether (30ml.). The mixture was refluxed for 3 hours and cooled. Excess hydride was decomposed by cautious addition of water. After filtration from the inorganic salts, the ether was distilled, leaving a white solid which was sublimed in vacuo to give 9-bicyclo(3.3.2)decanol (3.5g., 95%), m.p. 213-215°. (The literature ²⁹ g vs m.p. 213-215°).

IR(cm^{-1}): 3621, 2982, 2910, 1486, 1471, 1453, 1029.

NMR(τ): 5.90, $W_{1/2} = 20Hz$. (1H); 7.50 (br., 2H); 8.25 (sharp, 1H); 8.33 (1H).

9-Bicyclo(3.3.2)decene

Ethyl chloroformate (0.9ml.) was added over 2 minutes to a stirred solution of 9-bicyclo(3.3.2)decanol (900mg.) in pyridine (5ml.), cooled in an ice bath. The mixture was stoppered and allowed to stand for 24 hours at 0°, then poured onto a mixture of ice and 2N hydrochloric acid, and extracted with ether (3x20ml.). The combined ethereal extracts were washed twice with aqueous copper sulphate solution and dried. Distillation of the solvent gave crude 9-allyloxybicyclo(3.3.2)decane which was pyrolysed at 300° for 45 minutes. The crude product was then adsorbed on alumina (10g.) from pentane; elution with pentane yielded a white solid which was sublimed in vacuo and then recrystallized from methanol to give 9-²⁹bicyclo(3.3.2)decene (380mg., 48%), m.p. 126-128°. (The literature gives m.p. 128.4-130°). The product was homogenous to GLC (50), TSP capillary column, 100°).

IR(cm.⁻¹): 3022, 2920, 2862, 1655, 1425, (v. weak shoulder), 1459, 1447, 1117, 1092, 609, 270.

IR(KBr): shoulder at 1425 absent.

NMR(τ): 4.13 (quartet, 2H); 7.55 (br., 2H); 6.45 (12H).

¹³C NMR(δ): 129.76 (C9, C10), 33.44 (C1, C5), 28.45 (C2, C4, C6, C8), 22.98 (C3, C7).

9-Bicyclo(3.3.2)decyl p-toluenesulphonate

The following procedure was employed in the preparation of all tosylates. To a solution of 9-bicyclo(3.3.2)decanol (1.6g.)

in anhydrous pyridine (10ml.) was added recrystallised p-toluene sulphonyl chloride (2.2g.). The mixture was allowed to stand at 0° for 24 hours, and then poured into ice water. The mixture was extracted with ether (3x20ml.), and the extracts were washed with aqueous copper sulphate solution until all pyridine had been removed, and then dried. The solvent was removed in vacuo at 0°, to give a white solid which was recrystallised from ether/light petrol (20:80) at 0° to give 9-bicyclo(3.3.2)decyl p-toluenesulphonate (3g., 85%), m.p. 66-68°. (The literature ^{29,35} gives m.p. 66-68°).

IR(cm.⁻¹): 3076, 3042, 2920, 2862, 1918, 1803, 1600, 1497, 1485, 1453, 1369, 1309, 1291, 1260, 1139, 1178, 1100, 1025, 712, 583, 568.

EMR (C₆H₅)₃N): AA'BB' quartet centred at 2.33 (4H): 5.15 (mult., 1H); 7.55 (sharp, 3H); 8.4 (16H).

Reaction of 9-bicyclo(3.3.2)decyl tosylate with potassium
tert.-butoxide

A solution of 9-bicyclo(3.3.2)decyl tosylate (2.2g.) in dimethyl sulphoxide (20ml.) was added slowly to a stirred solution of potassium tert.-butoxide (2.4g.) in dimethyl sulphoxide (20ml.); and the resultant green solution was heated at 60° for 30 minutes, then cooled, poured into water and extracted with pentane (4x20ml.). The solvent was distilled from dried (basic alumina) solution to give a white solid, the GLC (PSEF, 50a. capillary column, 100°) of which showed the presence of 9-bicyclo(3.3.2)decene, and a second component of longer

retention time. The quantity of this second component varied from experiment to experiment - usually it was no more than 10%, but on one occasion it was the major product. This by-product was not isolated, but the NMR spectrum of the mixture exhibited olefinic resonances at higher field than 9-bicyclo(3.3.2)decene.

Reaction of 9-bicyclo(3.3.2)decanone with sodium borohydride

Sodium borohydride (250mg.) was added to a stirred solution of 9-bicyclo(3.3.2)decanone (500mg.) in methanol (30ml.). Stirring was continued for half an hour, then excess borohydride was destroyed with glacial acetic acid. The mixture was then poured into water and extracted with ether (3x30ml.). After drying, the solvent was distilled to give a solid, from which 9-bicyclo(3.3.2)decanol (100g., 20%) was obtained by vacuum sublimation. There was also a non-volatile residue whose identity could not be established.

Attempted catalytic reduction of 9-bicyclo(3.3.2)decanone

A solution of 9-bicyclo(3.3.2)decanone (500mg.) and perchloric acid (1ml.) in glacial acetic acid was stirred with 5% rhodium on charcoal catalyst under a hydrogen atmosphere for 2 days. There was no hydrogen uptake and the ketone was recovered unaltered. Identical reaction conditions, using the same catalyst sample, were found to reduce bicyclo(3.3.2)dec-2(3)-ene-9-one to 9-bicyclo(3.3.2)decanone in 30 minutes. This reaction is reported ³⁵ to require 18 hours using 5% palladium on charcoal.

Bicyclo[3.3.2]dec-2(3)-ene-9-one

Bicyclo[3.3.1]non-2-ene-9-one (20 g.) and triethyloxonium fluoroborate (50 g.) were dissolved in anhydrous methylene chloride (450 ml.) under a blanket of dry nitrogen, and the mixture was cooled to 0°. Ethyl diazoacetate (30 ml.) was then added with stirring over 1 hour. Stirring was continued for 3 hours at 0° and for a further 2 hours at room temperature. Saturated sodium bicarbonate solution (500 ml.) was added, the mixture was stirred for 1 hour, and the organic layer was separated and dried. After evaporation of the solvent, the residue was taken up in methanol, treated with potassium hydroxide (20 g.) and stirred and refluxed for 5 hours, then diluted with water (1 l.) and extracted with pentane (3x100 ml.). The combined organic extracts were washed with water, dried, and the solvent was distilled. The residual white solid was sublimed in vacuo to give bicyclo[3.3.2]dec-2(3)-ene-9-one (14 g., 65%), m.p. 94-96°. (No m.p. is quoted in the literature^{35,45} preparations of this compound.) GLC (carbowax 20M, 50' 30T, 150°) showed two components in equal amounts.

IR(cm^{-1}): 3390, 3020, 2935, 1704, 1660, 1457, 1448, 1429, 1410, 1401, 1375, 1361, 690.

The isomeric ketones could be separated by chromatography on alumina.

Bicyclo[3.3.2]dec-2-ene-9-one

This was the faster running compound on alumina, but the slower on GLC.

NMR(τ): 3.75-4.63 (mult., 2H); 6.75 (br., 1H); 7.37, 7.41, 7.54 (mults., 5H)
8.28 (mult., 6H).

Bicyclo[3.3.2]dec-2-ene-10-one

NMR(τ): 4.11-4.19 (mult., 2H); 7.2-7.8 (6H); 8.21 (6H);

2-Bicyclo[3.3.2]decene

Bicyclo[3.3.2]dec-2(3)-ene-9-one (10 g.) and hydrazine hydrate (100%, 4.2 ml.) were added to a solution of sodium (3.5 g.) in digol (160 ml.). The mixture was warmed at 80° for 1 hour, and then refluxed for 8 hours, during which the product sublimed into the condenser. The sublimed product was washed from the condenser with pentane, the pentane solution was washed with water, dried over basic alumina, and the solvent was distilled to leave 2-bicyclo[3.3.2]decene (7.8 g., 86%), m.p. 114-116°.

IR(cm^{-1}): 3011, 2915, 1655, 1467, 1452, 1448, 1429, 1071, 687.

NMR(τ): doublet centered at 4.35(2H); 7.43(br.), 7.69(sharp)(4H); 8.4(1OH).

exo-2-Hydroxybicyclo[3.3.2]dec-3-ene

2-Bicyclo[3.3.2]decene (500 mg.), selenium dioxide (300 mg.), and acetic anhydride (0.16 ml.) were dissolved in glacial acetic acid (5 ml.). The mixture was heated under reflux for 90 minutes, cooled, diluted with pentane and filtered through celite. The filtrate was washed with saturated aqueous sodium bicarbonate (3x20 ml.), saturated aqueous sodium thiosulphate (2x10 ml.), dried, and the solvent was distilled off, leaving crude exo-2-acetoxybicyclo[3.3.2]dec-3-ene as a yellow oil (690 mg.).

IR(cm^{-1}): 3020, 2930, 1735, 1660, 1458, 1448, 1371, 1230, 1050, 961, 922, 899.

The crude acetate (680 mg.) and sodium hydroxide (275 mg.) were dissolved in aqueous methanol (50:50, 10 ml.) and heated under

reflux for three hours. The cooled reaction mixture was diluted with brine and extracted with ether (3x15 ml.). The combined extracts were washed with 2N sulphuric acid and dried. Distillation of the solvent yielded a partially crystalline mass from which a white solid was obtained by vacuum sublimation. Purification by chromatography on alumina followed by sublimation gave exo-2-hydroxybicyclo[3.3.2]dec-3-ene (300 mg., 55%), m.p. 132-134°.

Found: C, 78.70; H, 10.55. $C_{10}H_{16}O$ requires C, 78.90; H, 10.60%.

IR(cm^{-1}): 3620, 3018, 2924, 2869, 1655, 1467, 1456, 1400, 1350, 1051, 935.

NMR(τ): doublet at 4.33(2H); 5.73, $J_1=11$ Hz. (1H); 7.42(sh., disappears with D_2O , 1H); 8.01, 8.30, 8.52, 8.70 (12H).

M^+ : m/e 152.

A small portion was reduced with hydrogen over 5% palladium on charcoal catalyst to give exo-2-bicyclo[3.3.2]decanol, identical in all respects with an authentic sample, thus establishing the exo configuration of the hydroxyl group.

Bicyclo[3.3.2]dec-3-ene-2-one

The following procedure was used for all oxidations of alcohols to ketones.

Jones chromic acid⁰² (0.2 ml.) was added over 5 minutes to a solution of exo-2-hydroxybicyclo[3.3.2]dec-3-ene (100 mg.) in ether (15 ml.), cooled in an ice bath. The reaction mixture, maintained at 0°, was then stirred vigorously for 1 hour. Granular anhydrous potassium carbonate (1 g.) was then added, the stirring was continued

for a further 10 minutes; then the ethereal solution was filtered and the solvent was distilled off. Vacuum sublimation of the residue gave bicyclo[3.3.2]dec-3-ene-2-one (89 mg., 90%), m.p. 96 - 98°.

Found: C, 79.90; H, 9.40. $C_{10}H_{14}O$ requires C, 79.95; H, 9.40%.

IR(cm^{-1}): 3028, 2946, 2871, 2860, 1688, 1620, 1458, 1449, 1400, 1380, 1360, 1339, 1310, 1275, 1193, 1162, 1142, 1119, 940.

NMR(τ): 3.56 (octuplet, AB part of AEX system, $J_{AB}=12$ Hz., 2H);
7.12 (2H); 8.16, 8.51 (10H).

M^+ : m/e 150.

exo-2,3-Epoxybicyclo[3.3.2]decane

To solution of 2-bicyclo[3.3.2]decene (8 g.) in anhydrous methylene chloride (60 ml.) was added over half an hour a solution of m-chloroperbenzoic acid (85%, 14 g.) in methylene chloride (160 ml.). The solution was stirred at room temperature for a further hour, then aqueous sodium metabisulphite solution was added till all oxidant had been destroyed. The separated organic layer was washed with saturated aqueous sodium bicarbonate (3x100 ml.), and dried; then the solvent was distilled and the waxy residue was sublimed in vacuo to give exo-2,3-epoxybicyclo[3.3.2]decane (8 g., 90%), m.p. 196 - 198°.

Found: C, 78.95; H, 10.50. $C_{10}H_{16}O$ requires C, 78.90; H, 10.60%.

IR(cm^{-1}): 2909, 1458, 1428, 1373, 1325, 1175, 1095, 1044, 953, 938, 900.

NMR(τ): 7.07 (quartet, 2H); 7.36 (1H); 7.89, 7.94, 8.27, 8.40 (13H).

M^+ : m/e 152.

exo-2-Bicyclo[3.3.2]decanol

exo-2,3-Epoxybicyclo[3.3.2]decane (1.52 g.) dissolved in anhydrous ether (10 ml.) was added to a stirred slurry of lithium aluminium hydride (400 mg.) in anhydrous ether (10 ml.), and heated under reflux for five days. Excess hydride was destroyed by the cautious addition of water, the ethereal solution was filtered, the inorganic salts were washed with ether, the ether fractions were combined and the ether was distilled off, leaving a waxy solid which was sublimed in vacuo to give exo-2-bicyclo[3.3.2]decanol (1.39 g., 90%), m.p. 166 - 169°, identical with an authentic sample.
IR(cm^{-1}): 3622, 2920, 2868, 1485, 1464, 1451, 1068, 990, 987, 975.
NMR(τ): 6.23, $\frac{W_1}{2} = 12$ Hz. (1H); 7.55(sh., exchanges with D_2O , 1H); 8.51 (16H).

2-Bicyclo[3.3.2]decanone

exo-2-Bicyclo[3.3.2]decanol (1.25 g.) was oxidised in ethereal solution in the usual manner. After work up, the product was sublimed to give 2-bicyclo[3.3.2]decanone (1.1 g., 88%), m.p. 174 - 176°.
IR(cm^{-1}): 3380, 2924, 2872, 1699, 1464, 1453, 1442, 1368, 1360, 1348, 1320, 1304, 1280, 1210, 1173, 1158, 1142, 1103, 927.
NMR(τ): 7.2 - 7.9 (5H); 7.9 - 8.85 (11H).

exo-3-Bicyclo[3.3.2]decanol

A solution of 2-bicyclo[3.3.2]decene (6 g.) in anhydrous tetrahydrofuran (30 ml.) was cooled to 0° and treated with a 1N solution of borane in tetrahydrofuran (16.25 ml.) over 15 minutes,

and then stirred at room temperature overnight. The reaction mixture was again cooled to 0°, and then treated sequentially with 3N sodium hydroxide solution (8ml.) and hydrogen peroxide (30%, 8 ml.), the latter over a period of 15 minutes. The reaction mixture was stirred for 1 hour at room temperature and then extracted with pentane (3x35 ml.); the combined extracts were washed with water, dried and concentrated. The reaction product was adsorbed onto alumina from the concentrated pentane solution and elution with pentane furnished a mixture of 2-bicyclo[3.3.2]decene and bicyclo[3.3.2]decane (500 mg.). Elution with light petrol/ether (50:50) furnished a mixture of exo-2- and exo-3-bicyclo[3.3.2]decanols (4.5 g.) which was adsorbed on alumina (150 g., neutral, grade 1) and eluted with a mixture of light petrol and ether (50:50). The less polar exo-2-bicyclo[3.3.2]decanol (450 mg.) was eluted first, and was identical with a sample as previously described. Further elution gave mixtures of the two alcohols in varying amounts. Finally, elution furnished exo-3-bicyclo[3.3.2]decanol (350 mg.), m.p. 138 - 140°. (The literature³⁵ gives m.p. 138 - 140°.)

IR(cm^{-1}): 3626, 2920, 1478, 1469, 1452, 1033, 1018.

100 MHz. NMR(τ): 5.82 (septuplet, $J_{AX}=11$ Hz., $J_{BX}=5$ Hz., 1H); 7.84, 8.26, 8.36 (17H).

Further amounts of exo-3-bicyclo[3.3.2]decanol could be obtained by repeated chromatography of the alcohol mixture.

3-Bicyclo[3.3.2]decanone

exo-3-Bicyclo[3.3.2]decanol (250 mg.) was oxidized with Jones⁹² chromic acid in the usual manner. Sublimation of the product furnished

3-bicyclo[3.3.2]decanone (230 mg., 87%).

Semicarbazone: m.p. 215 - 217^o.

IR(cm^{-1}): 2927, 1705(sh.), 1692, 1462, 1450, 1425, 1349, 1174.

220 MHz. NMR(τ): 7.47 (octet, AB part of two identical ABX systems,

$J_{AB} = 17 \text{ Hz.}$, $J_{AX} = 3 \text{ Hz.}$, $J_{BX} = 5 \text{ Hz.}$, 2H); 7.71 (2H);

8.07 (4H); 8.1 - 8.8 (6H).

3-Deutero-3-bicyclo[3.3.2]decanol

A solution of 3-bicyclo[3.3.2]decanone (100 mg.) in anhydrous ether (10 ml.) was added to a stirred slurry of lithium aluminium deuteride (45 mg.) in ether (10 ml.), and the mixture was refluxed with continuous stirring for 3 hours, with rigorous exclusion of moisture. Excess deuteride was destroyed by the careful addition of water, and the ethereal solution was filtered from the inorganic salts which were washed once with ether (10 ml.). The filtrate and washings were combined and the solvent was distilled off, to leave 3-deutero-3-bicyclo[3.3.2]decanol (87 mg., 88%), of exo:endo ratio 40:60.

IR(cm^{-1}): 3613, 2920, 2368, 2150, 1464, 1450, 1380, 1073, 1047.

NMR(τ): No O3 carbonyl proton resonance.

3-Deutero-3-bicyclo[3.3.2]decyl tosylate

3-Deutero-3-bicyclo[3.3.2]decanol (80 mg.) was dissolved in pyridine (0.5 ml.) and treated with tosyl chloride (110 mg.).

The normal work-up procedure furnished the mixed 3-deutero-3-bicyclo[3.3.2]decyl tosylates (120 mg., 79%) as a white solid.

IR(cm^{-1}): 3078, 3042, 2930, 2877, 2205, 1919, 1600, 1498, 1460, 1452, 1370, 1259, 1190, 1130, 1102, 1020, 960, 915, 871, 669.

NMR(τ). No C β carbinyl proton resonance.

3,3-Dideuterobicyclo[3.3.2]decane

3-Deutero-3-bicyclo[3.3.2]decyl tosylate (120 mg.) in anhydrous ether (10 ml.) was added to a stirred slurry of lithium aluminium deuteride (50 mg.) in ether (10 ml.) and the mixture was refluxed for 24 hours. Excess deuteride was destroyed by careful addition of water and the ethereal solution was filtered from the inorganic salts which were washed with a further portion of ether (10 ml.). The filtrate and washings were combined and analysed by GLC (OV 1, 80 $^{\circ}$) which revealed two components in the ratio 60:40. Comparison with authentic (undeuterated) samples showed that the minor component was 3,3-dideuterobicyclo[3.3.2]decane and the major component was 3-deutero-2-bicyclo[3.3.2]decane. The two components were separated by preparative layer chromatography on silver nitrate/silica gel (25:75); the plate was developed with pentane. The fast moving material was the required 3,3-dideuterobicyclo[3.3.2]decane (24 mg., 20%).

IR(cm^{-1}): 2900, 2870, 2850, 2150, 1458, 1442.

M $^+$: m/e 140, m/e 139, m/e 138. $d_2 = 93.1\%$, $d_1 = 5.2\%$, $d_0 = 1.7\%$.

No. of deuterium atoms per molecule = 1.914.

2,2-Dideuterobicyclo[3.3.2]decane

This was prepared by an identical procedure to 3,3-dideuterobicyclo[3.3.2]decane. Thus, 2-bicyclo[3.3.2]decanone (100 mg.) was reduced in ether solution with lithium aluminium deuteride (45 mg.). The resultant 2-deutero-2-bicyclo[3.3.2]decanol was treated with tosyl chloride (110 mg.) in the usual manner to furnish the mixed 2-deutero-2-bicyclo[3.3.2]decyl tosylates, which were treated with lithium aluminium deuteride (50 mg.) in ether solution. GLC analysis of the reaction product again showed two components in the ratio 60:40. Preparative layer chromatography on silver nitrate/silica gel (25:75) using pentane as the developing solvent furnished the minor, less polar component, 2,2-dideuterobicyclo[3.3.2]decane (30 mg., 25%).

IR(cm^{-1}): 2900, 2850, 2150, 1485(sh.), 1465, 1455.

M^+ : m/e 140, m/e 139, m/e 138. $d_2 = 94.9\%$, $d_1 = 4.4\%$, $d_0 = 0.6\%$.

No. of deuterium atoms per molecule = 1.942.

0,0-bis(trimethylsilyl)bicyclo[3.3.2]dec-9-ene-9,10-diol

Sodium (720 mg.) was melted under hot xylene (75 ml.), under a blanket of dry nitrogen; and dispersed by rapid stirring. Trimethylsilyl chloride (6.78 g.) followed by diethyl cyclo-octane-1,5-dicarboxylate (1 g.) were then added and the reaction mixture was heated under reflux for one hour with vigorous stirring. The cooled mixture was filtered and the solvent was distilled to leave a brown semi-solid with a strange smell. Short path distillation furnished 0,0-bis(trimethylsilyl)bicyclo[3.3.2]dec-9-ene-9,10-diol (70 mg., 6%).

as a viscous, colourless oil, b.p. 110 - 112°/0.1 mm.

IR(cm^{-1}): 2990, 2960, 2925, 2885, 2860, 1489, 1453, 1301, 1250, 1052, 910.

NMR(τ , relative to benzene as internal standard): 8.2 (14H); 9.9 (6H).

Reaction of bicyclo[3.3.1]non-2-ene-9-one with diazomethane

Bicyclo[3.3.1]non-2-ene-9-one (20 g.), potassium hydroxide (9 g.) and water (30 ml.) were dissolved in methanol (200 ml.) and cooled in an ice/salt bath. A solution of N-nitroso-N-methyl-p-toluene-sulphonamide (60 g.) in methanol (450 ml.) was added slowly to the stirred mixture, the reaction temperature being maintained below 20°. After being stirred overnight, the reaction mixture was diluted with water (1.5 l.) and extracted with ether (3x200 ml.). Distillation of the solvent from the combined extracts gave an oily product, a mixture of methyl tosylate, 9-epoxymethylene-bicyclo[3.3.1]non-2-ene, and bicyclo[3.3.2]dec-2(3)-ene-9-one. The mixture was dissolved in ethanol (100 ml.) and a solution of potassium hydroxide (10 g.) in water (70 ml.) was added and the mixture was refluxed for 15 hours, then diluted with water (1.5 l.) and extracted with pentane (3x150 ml.). The combined organic extracts were washed with water and dried, and the solvent was distilled off leaving an oily product. GLC (carbowax 20 M, 50' SCOT column, 150°) analysis revealed a mixture of bicyclo[3.3.2]dec-2(3)-ene-9-one (70%) and another product (25%). This mixture was adsorbed on alumina

from light petrol and eluted with ether/light petrol (5:95) to give the byproduct (4.75 g., 21%) and bicyclo[3.3.2]dec-2(3)-ene-9-one (10.75 g., 49%), m.p. 94 -96°. The by-product is probably bicyclo[3.3.1]non-2-ene-9-carboxaldehyde, produced by rearrangement of 9-epoxymethylenebicyclo[3.3.1]non-2-ene.

exo-2-Hydroxybicyclo[3.3.2]dec-6(7)-ene

Redistilled trifluoroacetic acid (25 ml.) was added over 30 minutes to a stirred solution of exo-2,3-epoxybicyclo[3.3.2]decane (2.5g.) in pentane (30 ml.), cooled to 0° in an ice bath. After stirring for 4 hours, a solution of sodium hydroxide (20 g.) in water (30 ml.) was added over 1 hour, and then the mixture was stirred for a further 15 hours to hydrolyse the trifluoroacetate esters. The organic layer was then separated, and the aqueous layer was extracted with ether (2x20 ml.); the combined organic extracts were washed with water and dried over potassium carbonate. Distillation of the solvent followed by vacuum sublimation of the residue gave exo-2-hydroxybicyclo[3.3.2]dec-6(7)-ene (1.82 g., 87%), m.p. 135 - 142°.

Found: C, 77.90; H, 10.40. $C_{10}H_{16}O$ requires C, 78.90; H, 10.60%.

IR(cm^{-1}): 3625, 3017, 2928, 1654, 1457, 1423, 1346, 1183, 1080, 1045, 952.

NMR(τ): 4.4 (2H); 6.0 (1H); 7.58 (sh., exchanges with D_2O , 1H);
7.57 (2H); 8.3 (1OH).

M^+ : m/e 152. ($M - H_2O$) $^+$: m/e 134.

GLC analysis (TCEP, 50m. capillary column, 135°) showed two components in the ratio 73:27; the retention times were 44.2 and 46.3 minutes respectively.

The corresponding acetate was a clear oil;

IR(cm^{-1}): 3017, 2930, 1740, 1655, 1450, 1370, 1250, 1083, 1035, 963.

Bicyclo[3.3.2]dec-2-one-6(7)-ene

exo-2-Hydroxybicyclo[3.3.2]dec-6(7)-ene (1 g.) was oxidized by the usual method. Vacuum sublimation of the product gave bicyclo[3.3.2]dec-2-one-6(7)-ene (885 mg., 88%), m.p. 103 - 117°.

Found: C, 79.90; H, 9.35. $C_{10}H_{14}O$ requires C, 79.95; H, 9.40%.

IR(cm^{-1}): 3380, 3023, 2938, 2871, 1701, 1671, 1468, 1450, 1431, 1350, 1163, 1133.

100 MHz. NMR(τ): 4.30 (2H); 6.94 (0.3H); 7.5, 8.2 (mults., 13.7H).

M^+ : m/e 150.

Integration of the peak at 6.94 τ in the NMR with reference to the olefinic resonance as a standard 2 protons showed that the mixture contained bicyclo[3.3.2]dec-2-one-6-ene (70%) and bicyclo[3.3.2]dec-2-one-7-ene (30%).

Wolff-Kishner reduction of bicyclo[3.3.2]dec-2-one-6(7)-ene

Bicyclo[3.3.2]dec-2-one-6(7)-ene (100 mg.) was reduced by the method described for the synthesis of bicyclo[3.3.2]decane. The sole product was 2-bicyclo[3.3.2]decene, thus establishing the position of the double bond.

Hydrogenation of exo-2-hydroxybicyclo[3.3.2]dec-6(7)-ene

exo-2-Hydroxybicyclo[3.3.2]dec-6(7)-ene (100 mg.) was dissolved in ethanol and reduced with hydrogen over 5% palladium on charcoal catalyst. When hydrogen uptake ceased, the solution was filtered through glass fibre filter paper and the solvent was evaporated.

Sublimation of the residue gave exo-2-bicyclo[3.3.2]decanol, identical with an authentic sample, thus establishing the exo configuration of the hydroxyl group.

Buffered Acetolysis of exo-2,3-epoxybicyclo[3.3.2]decane

A solution of exo-2,3-epoxybicyclo[3.3.2]decane (1 g.) and anhydrous sodium acetate (1.95 g.) in dry glacial acetic acid (31.25 ml.) was heated for 72 hours at 100° in a sealed tube. The cooled reaction mixture was poured into water and extracted with ether. The organic extracts were thoroughly washed with aqueous sodium bicarbonate, dried, and the solvent was removed to give a yellow oil (1.29 g., 89%), which was adsorbed on silica gel from light petrol. Elution with ether/light petrol (20:80) yielded first an unsaturated acetate fraction (593 mg., 47%) and secondly a diacetate fraction (697 mg., 42%).

Examination of unsaturated acetate fraction

GLC analysis (TCEP, 50 m. capillary column, 125°) showed four components to be present. Comparison with known materials by cross injection experiments showed that they were:- exo-2-acetoxibicyclo[3.3.2]dec-3-ene (6.5%), exo-2-acetoxibicyclo[3.3.2]dec-6(7)-ene, only partially resolved (41%), and an unknown material (1.4%). Reduction of the acetates to the corresponding alcohols with lithium aluminium hydride, followed by GLC analysis of the unsaturated alcohols (135°) showed the presence of

exo-2-hydroxybicyclo[3.3.2]dec-6-ene (23.5%), exo-2-hydroxybicyclo[3.3.2]dec-3(7)-ene, unresolved (22.5%), and an unknown product (1.5%). Catalytic reduction of the unsaturated alcohols with hydrogen, followed by GLC analysis showed that the minor product was neither exo-3-bicyclo[3.3.2]decanol, nor 9-bicyclo[3.3.2]decanol. The original unknown is tentatively assigned as exo-2-tricyclo[3.3.2.0^{3.7}]decyl acetate.

Examination of the diacetate fraction

GLC analysis (21% OV 1, 175°) showed five compounds. Their retention times relative to that of the unresolved unsaturated acetates as 1.00 together with their respective ratios were:-
1.53, 1%; 2.00, 4%; 2.32, 20%; 2.83, 1%; 3.13, 17%.

Pure samples of the two components could be obtained by preparative GLC (for 2.32) or by chromatography on silica (for both 2.32 and 3.13).

2.32

IR(cm^{-1}): 2930, 1739, 1466, 1450, 1370, 1232, 1067, 1034, 933, 905.
100 MHz. NMR(τ): Broad multiplet centered at 6.1 τ ; $J_{AX} = 5 \text{ Hz.}$, $J_{BX} = 10 \text{ Hz.}$, with sharp band at 6.13 τ superimposed (2H).
7.80 (br., 2H); 8.06 (sh., 6H); 8.4 (14H).

3.13

IR(cm^{-1}): 2938, 1740, 1459, 1370, 1230, 1100, 1050, 1035, 905.
NMR(τ): 4.95, $W_1 = 18 \text{ Hz.}$ (2H); 8.04 (sh., 6H); 7.20, 8.20 (16H).

2.32 is assigned as exo,exo-2,7-diacetoxibicyclo[3.3.2]decane.

3.13 is assigned as exo-2-endo-3-diacetoxibicyclo[3.3.2]decane.

Reduction of diacetate fraction with lithium aluminium hydride

The mixture of diacetates (100 mg.) in dry ether (5 ml.) was added to a stirred slurry of lithium aluminium hydride (40 mg.) in dry ether. Stirring was continued for 3 hours at room temperature, then water was added to destroy excess hydride. The inorganic salts were filtered off, washed with methylene chloride (2x10 ml.), the organic filtrates were combined and the solvents were evaporated, to leave a white solid (60 mg., 90%), a mixture of exo, exo-bicyclo(3.3.2)decan-2,7-diol and exo-2-endo-3-bicyclo(3.3.2)decandiol.

Reduction of the pure diacetates 2.32 and 3.13

2.32 and 3.13 (30 mg. of each) were both reduced with lithium aluminium hydride in an identical manner to that described above.

2.32 furnished exo,exo-bicyclo(3.3.2)decan-2,7-diol (18 mg., 90%) as a white solid.

IR(cm^{-1} , KBr): 3470, 2900, 1468, 1450, 1260, 1090, 1030, 1002, 988, 963, 800, 395.

NMR(CHCl_3 , τ): 6.0, 6.3(2H); 6.8(broad singlet, 2H); 7.85, 8.13, 8.3, 8.51 (14H).

3.13 furnished exo-2-endo-3-bicyclo(3.3.2)decandiol (16 mg., 87%) as a white solid.

IR(cm^{-1} , KBr): 3450, 2920, 1460, 1260, 1079, 1050, 1020, 1000, 943, 901, 800.

NMR(CHCl_3 , τ): 6.0, $W_{\frac{1}{2}} = 18 \text{ Hz.}$ (2H); 6.46(singlet, 2H); 7.80, 8.30, 8.70 (14H).

Reaction of diol mixture with periodic acid

The diol mixture (40 mg.) was added to a solution of potassium

periodate (920 mg.) and 2N sulphuric acid (0.4 ml.) in water (5 ml.). The reaction mixture was stirred for 24 hours at room temperature, and then saturated with salt and extracted with methylene chloride (3x10 ml.). The combined organic extracts were washed with water, dried, and the solvent was evaporated, leaving a yellow oil which was treated with hydrogen peroxide (30%, 3 ml.) for 30 minutes. Saturated sodium bicarbonate solution was then added and the reaction mixture was stirred for 15 minutes and then extracted with methylene chloride. After washing and drying, the solvent was removed from the combined extracts to leave a white solid (18 mg., 46%). TLC analysis showed that this was only exo,exo-bicyclo(3.3.2)decan-2,7-diol (the less polar of the two diols). The more polar vicinal diol was no longer present, thus establishing the vic-diol structure for the more polar diol.

Reaction of exo-2,3-epoxybicyclo(3,3,2)decane with lithium diethylamide

A 2.2M solution of n-butyl lithium in hexane (2 ml.) was added to a solution of anhydrous diethylamine (0.22 ml.) in anhydrous benzene (2.5 ml.) under a blanket of dry nitrogen. The mixture was allowed to stand for 10 minutes, then a solution of exo-2,3-epoxy bicyclo(3.3.2)decane (260 mg.) in anhydrous benzene (2 ml.) was added, and the mixture was then heated under reflux for 48 hours. The cooled reaction mixture was poured into ice water and extracted with ether; the combined organic extracts were washed with water and ice cold 0.1 N hydrochloric acid, and then dried. Evaporation

of the solvent gave a solid which was sublimed in vacuo to give a white solid (140 mg., 54%), found to be identical in all respects with exo-2-hydroxybicyclo(3.3.2)dec-3-ene, as prepared by allylic oxidation of 2-bicyclo(3.3.2)decene.

A small sample of the product was oxidised with Jones' chromic acid⁹² in the usual manner to bicyclo(3.3.2)dec-2-one-3-ene, again identical in all respects with an authentic sample.

exo-2-Bicyclo(3.3.2)decyl tosylate

exo-2-Bicyclo(3.3.2)decanol (130 mg.) in pyridine (0.7 ml.) was treated with p-toluenesulphonyl chloride (180 mg.). The usual isolation procedure furnished the tosylate (200 mg., 71%), m.p. 70 - 72°. (The literature³⁵ gives m.p. 70 - 72°).

IR(cm^{-1}): 2920, 2867, 1600, 1497, 1462, 1452, 1379, 1190, 1180, 1101, 910, 669, 583, 569.

NMR(CDCl_3, τ): A_2B_2 quartet centered at 2.34 (4H); 5.3(mult., 1H); 7.55(sharp singlet, 3H); 7.8, 8.3(16H).

endo-3-Deutero-exo-2-bicyclo(3.3.2)decanol

To a stirred slurry of lithium aluminium deuteride (100 mg.) in anhydrous ether (5 ml.) was added exo-2,3-epoxybicyclo(3.3.2)decane (860mg.) in dry ether (10 ml.). The mixture was stirred and refluxed for 1 week. After destruction of excess deuteride by cautious addition of water, the usual isolation procedure gave a white solid. GLC analysis (4% Apiezon L, 150°) showed about 50% starting epoxide and 50% alcohol.

Chromatography on silica gel gave endo-3-deutero-exo-2-bicyclo(3.3.2)

decanol (400 mg., 48%), m.p. 166 - 168°.

IR(cm^{-1}): 3620, 2920, 2864, 2150, 1461, 1449, 1064, 990, 921.

M⁺: m/e 155, m/e 154. 90.7% d₁, 9.3% d₀.

No. of deuterium atoms per molecule = 0.907.

endo-3-deutero-exo-2-bicyclo(3.3.2)decyl tosylate

Treatment of endo-3-deutero-exo-2-bicyclo(3.3.2)decanol (175 mg.) with p-toluenesulphonyl chloride (245 mg.) in pyridine (1 ml.) in the usual manner furnished the tosylate as an oil which was crystallized at 0° from a pentane:ether mixture, m.p. 70 - 72° (290 mg., 83%).

IR(cm^{-1}): 3040, 2923, 2161, 1917, 1800, 1600, 1493, 1461, 1449, 1400, 1363, 1340, 1306, 1289, 1188, 1179, 1100, 951, 937, 900, 668, 580, 568.

Buffered Acetolysis of exo-2-bicyclo(3.3.2)decyl tosylate

Identical procedures were used for the acetolysis of both the labelled and unlabelled tosylates.

exo-2-Bicyclo(3.3.2)decyl tosylate (150 mg.) and fused sodium acetate (45 mg.) were dissolved in anhydrous glacial acetic acid (12 ml.). The solution was sealed into a Carius tube and heated at 40° for 3 days. The cooled reaction mixture was poured into water and extracted with pentane (3x10 ml.). The combined organic extracts were washed with saturated sodium bicarbonate solution and dried. The solution was concentrated, then examined by GLC (TCEP 50 m., 0.1" capillary column, 100° increasing to 135°), which showed five unidentified olefins,

2-bicyclo(3.3.2)decene (65%), two more unidentified olefins, five unidentified acetates, 1-bicyclo(3.3.2)decyl acetate (5.6%), exo-2-bicyclo(3.3.2)decyl acetate (5.4%), endo-2-bicyclo(3.3.2)decyl acetate (0.4%), and exo- & endo-3-bicyclo(3.3.2)decyl acetates (0.6% & 0.4% respectively). (See chapter 2, section (i), table 3.).

Conversion of the labelled solvolysis products to ketones.

After removal of all solvent from the products from the buffered acetolysis of endo-3-deutero-exo-2-bicyclo(3.3.2)decyl tosylate, the semi-solid residue was dissolved in anhydrous ether and treated with lithium aluminium hydride (30 mg.) at room temperature for 3 hours. Excess hydride was destroyed by careful addition of water, and the inorganic salts were filtered off. The filtrate was cooled in an ice bath and Jones' chromic acid⁹² (0.1 ml.) was added with stirring, which was continued for a further hour. Granular anhydrous potassium carbonate was then added, the ethereal solution was filtered, concentrated, and analysed by GLC (TCEP capillary column, 135°). Apart from the olefinic products which were unaltered, the main products were 1-bicyclo(3.3.2)decanol and 2-bicyclo(3.3.2)decanone.

Wash out of deuterium atoms α to the carbonyl group.

This procedure is known to wash out deuterium atoms α to a carbonyl group in the bicyclo(3.3.2)decane ring.³⁵

A solution of the ketonic solvolysis product (above) and clean sodium metal (20 mg.) in dioxane (2.5 ml.) and water (2 ml.) was

heated in a sealed ampoule at 80° for 5 days. The cooled reaction mixture was poured into water and extracted with pentane (3x10 ml.). The combined organic extracts were washed with water and dried; the solution was then concentrated and examined by combined GLC - mass spectrometry.

2-Bicyclo(3.3.2)decanone: M^+ : m/e 153, m/e 152. $d_1 = 32\%$; $d_0 = 68\%$.

Uncatalysed autoxidation of bicyclo(3.3.2)decane

A solution of bicyclo(3.3.2)decane (500 mg.) in redistilled pentane (25 ml.) was passed through a bed of basic alumina. The solution was then boiled under reflux for 16 hours while passing in oxygen. The pentane was then removed from the cooled reaction mixture and the solid residue was taken up in dry ether and treated with lithium aluminium hydride (25 mg.) for 1 hour. Excess hydride was destroyed with water, the inorganic salts were filtered off, and the ethereal solution was concentrated and examined by GLC (4% Apiezon L) which showed the presence of a trace of 1-bicyclo(3.3.2)decanol, together with the starting bicyclo(3.3.2)decane (99%).

Autoxidation of bicyclo(3.3.2)decane using cobalt acetate bromide catalyst

Freshly purified bicyclo(3.3.2)decane (140 mg.) and cobalt(II) acetate (50 mg.) were dissolved in glacial acetic acid (10 ml.).

A solution of hydrogen bromide in glacial acetic acid (15%, 1 ml.) was then added, and a stream of oxygen was passed through the reaction mixture which was heated under reflux for 16 hours. The cooled reaction mixture was poured into water and extracted with ether (3x15 ml.). The combined ethereal extracts were washed with saturated sodium bicarbonate solution and dried over potassium carbonate. Removal of the solvent furnished a brown solid (120 mg., 83%), which was added to a stirred slurry of lithium aluminium hydride (50 mg.) in ether. Usual work up

furnished a white solid, which was examined by GLC (4% Apiezon J).
Present were bicyclo(3.3.2)decane (93%) and 1-bicyclo(3.3.2)decanol (7%).

Attempted synthesis of 1,3,5,7-tetracarbomethoxybicyclo(3.3.2)
decane-2,6-dione

Dimethyl methylene malonate (4 g.) and 1,1,4,4-tetracarbomethoxybutane (4 g.) were dissolved in dry methanol (25 ml.) and added to a solution of sodium (677 mg.) in methanol (25 ml.). The mixture was heated under reflux with stirring for 24 hours, the methanol was distilled off, and the residue was treated with ice water and extracted with ether (2x20 ml.). The aqueous residue was then treated with cold 2N hydrochloric acid until precipitation ceased. The acidified aqueous layer was then extracted with ether (3x20 ml.), and the combined extracts were washed with water and dried. Removal of the solvent furnished a white gum; TLC showed at least two major components and three minor ones.

IR(cm^{-1}): 2910, 1740, 1720(sh.).

exo-2-Tosyloxybicyclo(3.3.2)dec-6(7)-ene

exo-2-Hydroxybicyclo(3.3.2)dec-6(7)-ene (400 mg.) was treated with *p*-toluenesulphonyl chloride (560 mg.) in pyridine (5 ml.).

Usual work up furnished the tosylate as an oil, which could be recrystallised at -80° , but remelted at approximately -10° .

IR(cm^{-1}): 3003, 2930, 1600, 1495, 1441, 1360, 1190, 1100, 903, 850, 817, 709, 671.

Attempted tosylate elimination reaction

A solution of exo-2-tosyloxybicyclo(3.3.2)dec-6(7)-ene (450 mg.) in dimethyl sulphoxide (8 ml.) was added to a solution of potassium

tert.-butoxide (900 mg.) in dimethyl sulphoxide (3 ml.). The green reaction mixture was stirred and heated for 30 minutes at 60°, then poured into ice water and extracted with pentane (4x10 ml.). The combined extracts were washed with water, dried and the pentane was removed by distillation to furnish a pale yellow oil with a strong smell (150 mg.).

IR(cm^{-1}): 3020, 2980, 2925, 2865, 1650, 1465, 1450, 1389, 1369, 1250, 1194, 1150, 1045.

GLC (SCOT column, Carbowax 20M, 120°) showed three components, tentatively assigned as bicyclo(3.3.2)deca-2,7-diene (17%), bicyclo(3.3.2)deca-2,6-diene (28%), and 2-bicyclo(3.3.2)dec-6(7)-enyl tert.-butyl ether (56%).

Dehydration of *exo*-2-hydroxybicyclo(3.3.2)dec-6(7)-ene

Redistilled thionyl chloride (from linseed oil, 0.66 ml.) was added to a stirred solution of exo-2-hydroxybicyclo(3.3.2)dec-6(7)-ene (400 mg.) in dry pyridine (16 ml.). The reaction mixture was heated at 40° for 18 hours, then poured into ice water and extracted with iso-pentane(3x15 ml.). The combined organic extracts were washed thoroughly with ice cold 2N hydrochloric acid and dried. The solution was concentrated and analysed by GLC (2% Carbowax 20M, 80°) which showed six major products, the least polar of which had the same retention time as the product assigned as bicyclo(3.3.2)deca-2,6-diene from the tosylate elimination reaction.

This component of the mixture was isolated by preparative GLC (10% Carbowax 20M, 140°) as a white crystalline solid with a strong smell (15 mg., 3.5%). From the spectral data it was assigned as

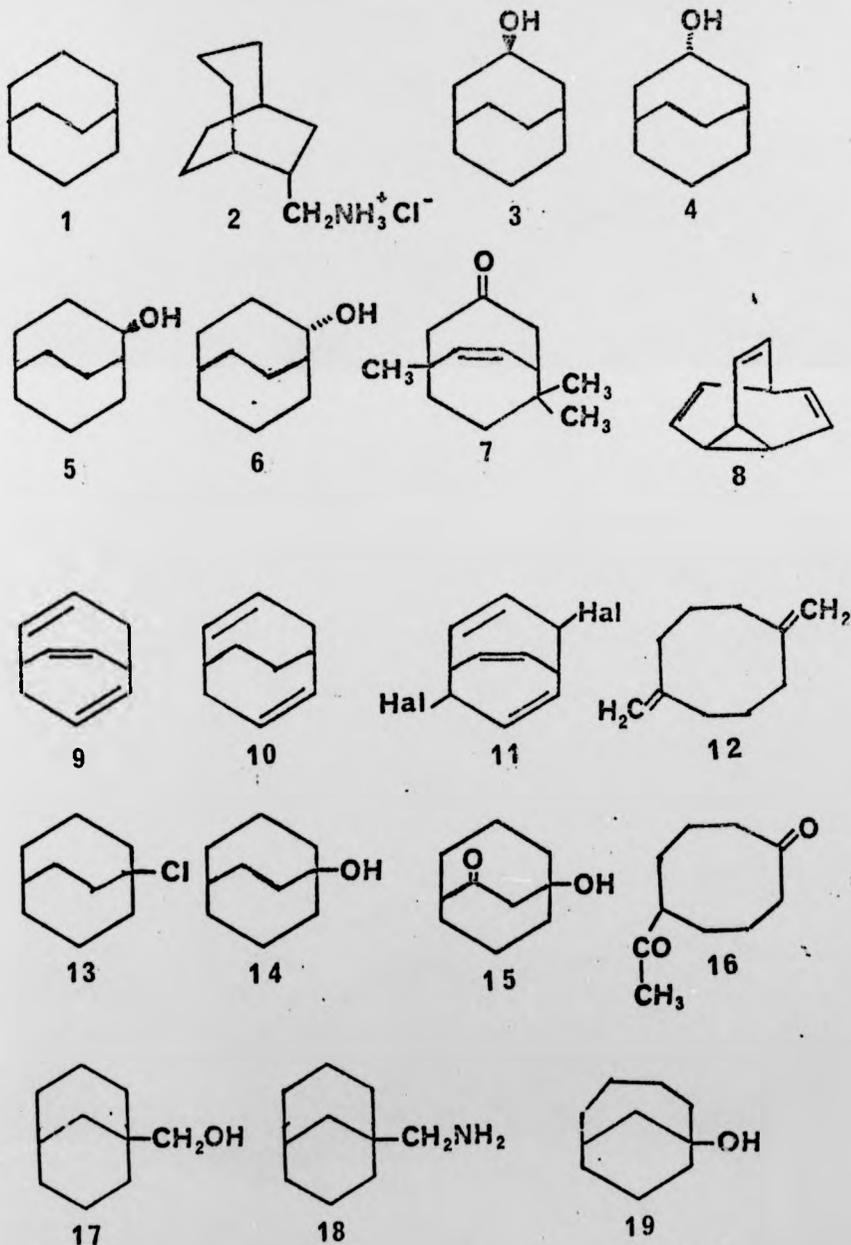
bicyclo(3.3.2)deca-2,6-diene.

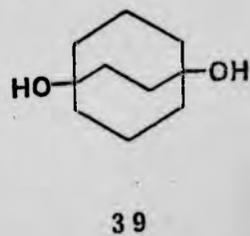
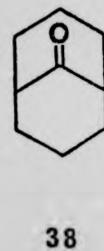
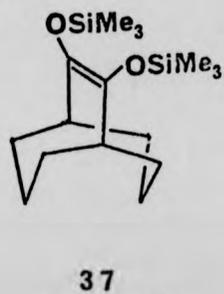
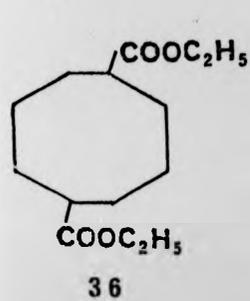
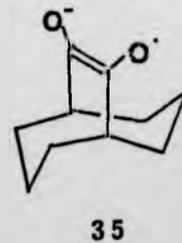
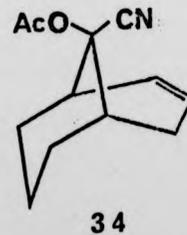
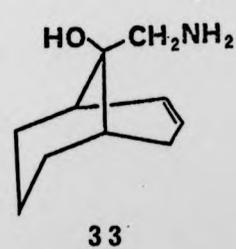
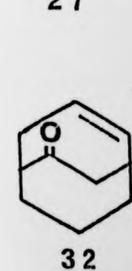
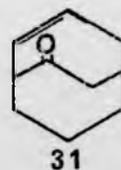
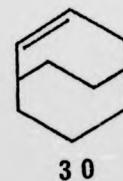
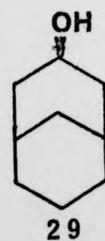
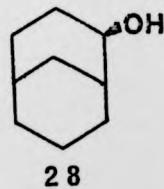
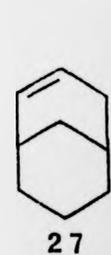
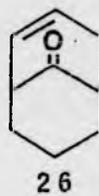
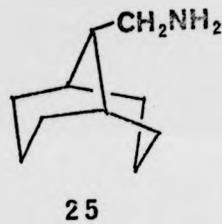
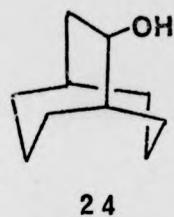
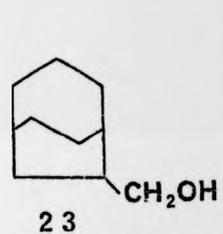
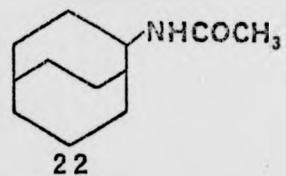
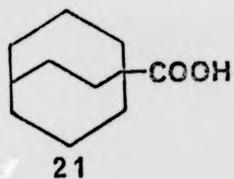
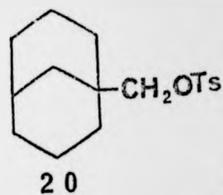
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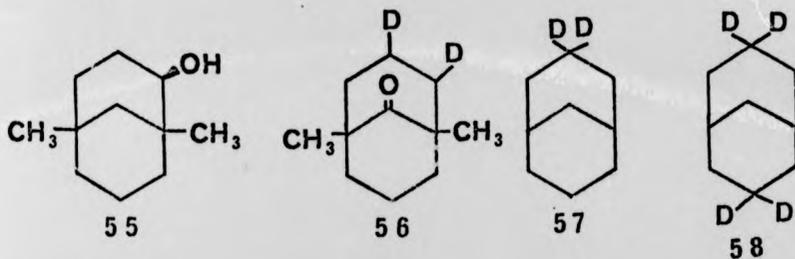
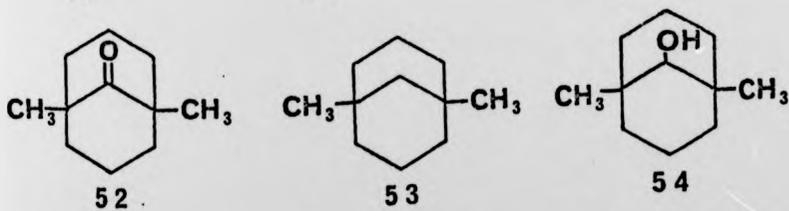
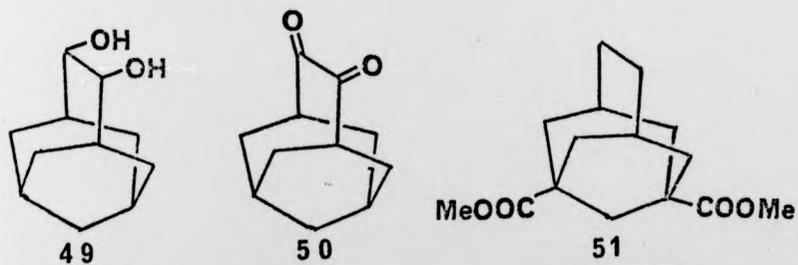
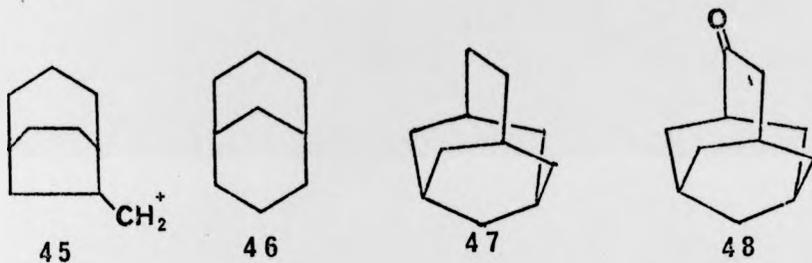
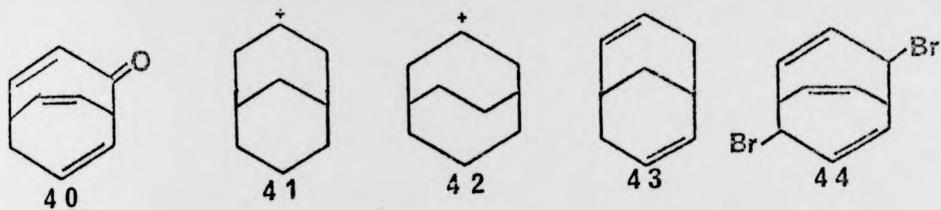
100 MHz. NMR(): 4.44(multiplet, band width 30 Hz., 4H); 7.50, 7.74,
7.97, 8.18 (multiplets, 10H).

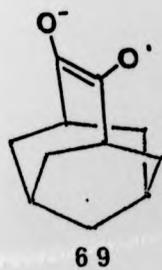
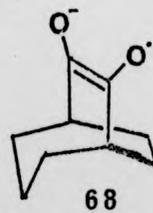
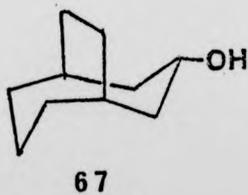
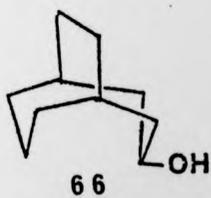
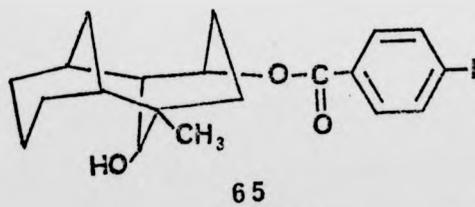
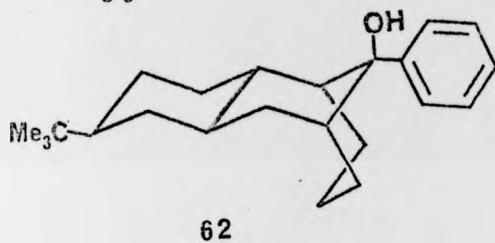
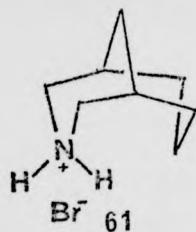
220 MHz. NMR(): 4.46 (two triplets, 4H); 7.4 - 8.3 (10H).

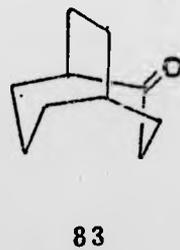
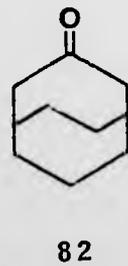
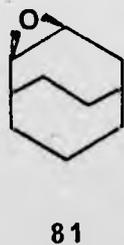
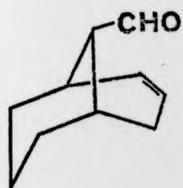
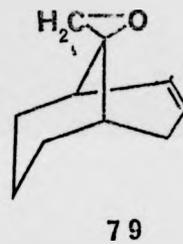
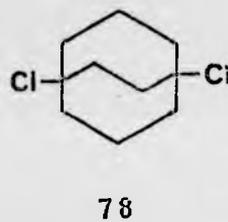
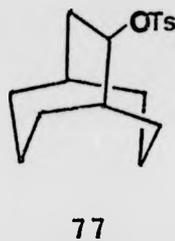
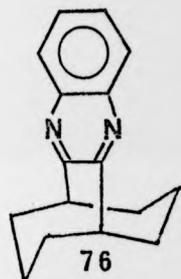
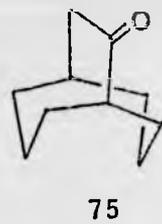
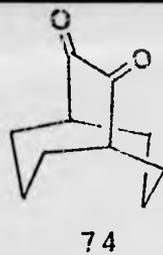
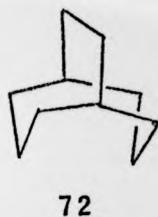
M^+ : m/e 134.









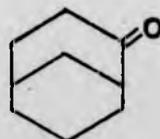
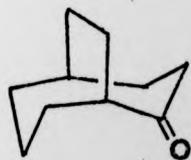


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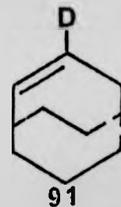
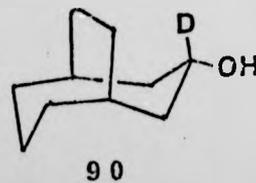
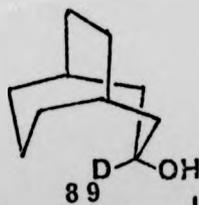
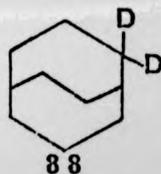


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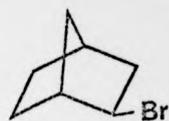
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167



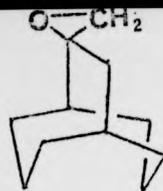
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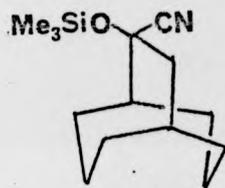
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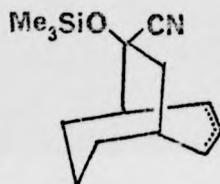
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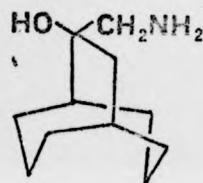
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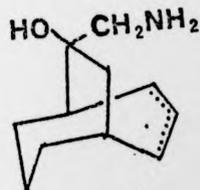
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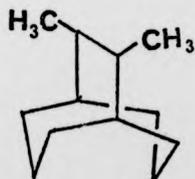
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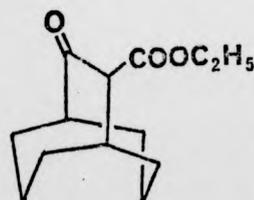
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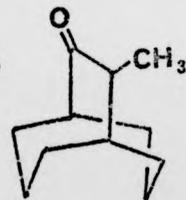
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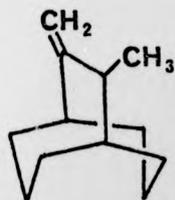
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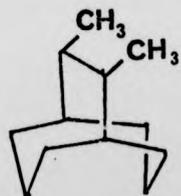
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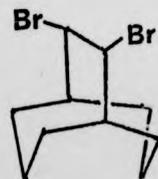
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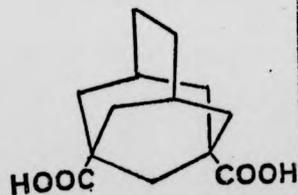
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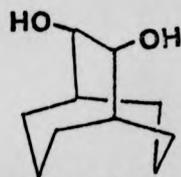
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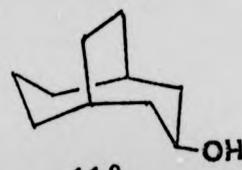
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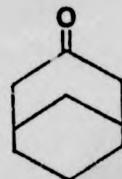
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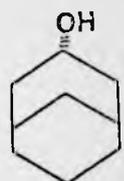


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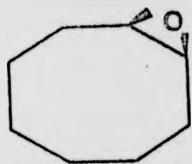


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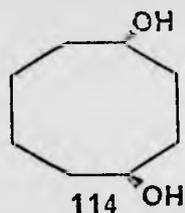
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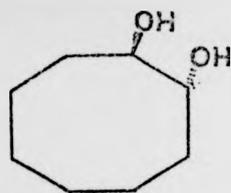
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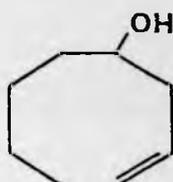
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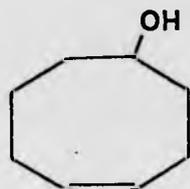
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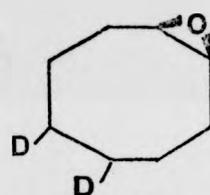
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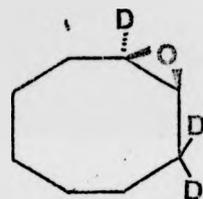
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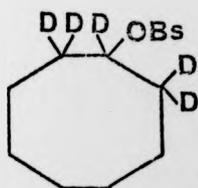
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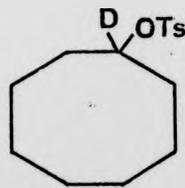
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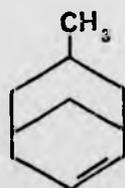
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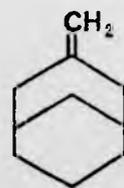
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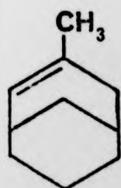
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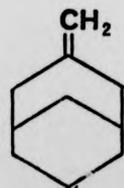
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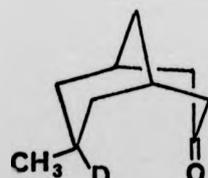
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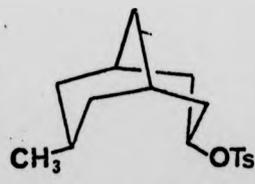
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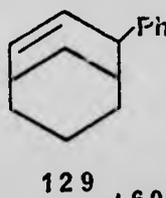
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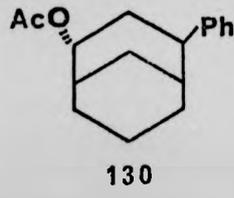
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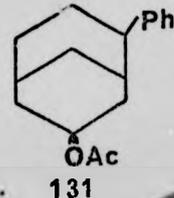
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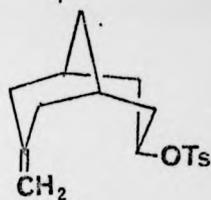


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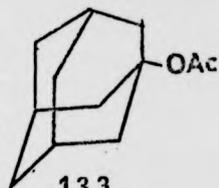


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132



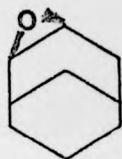
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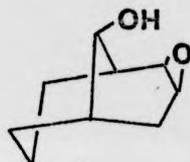
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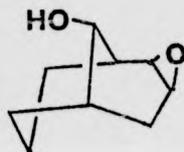
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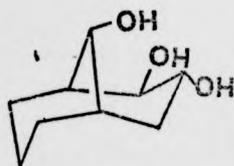
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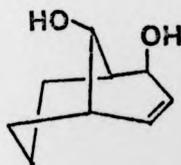
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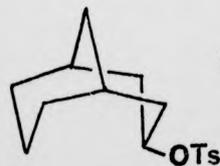
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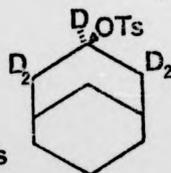
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141



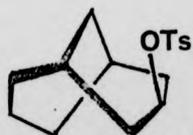
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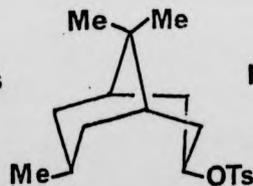
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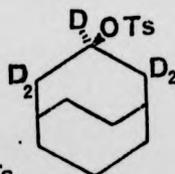
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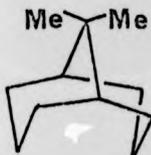
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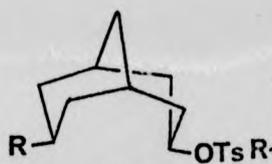
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147



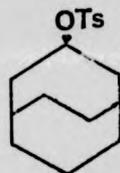
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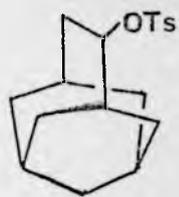


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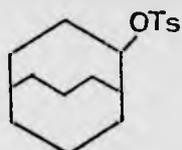


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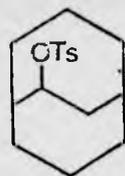
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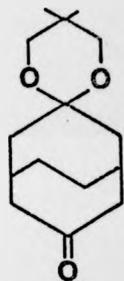
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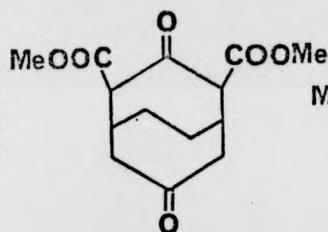
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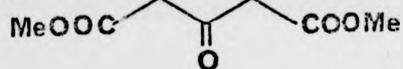
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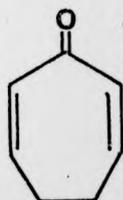
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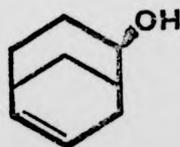
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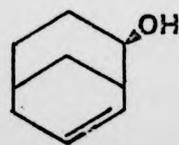
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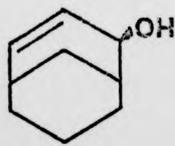
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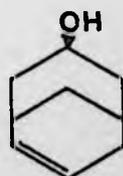
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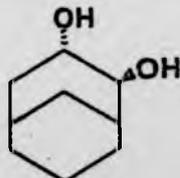
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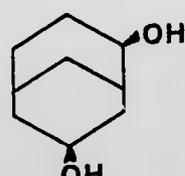
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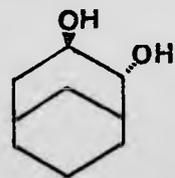
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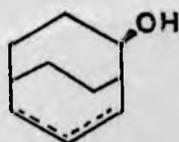
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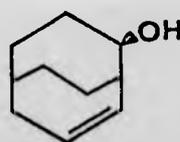
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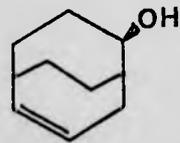
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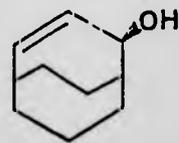
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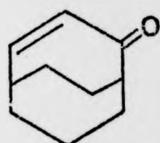


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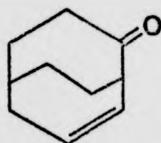


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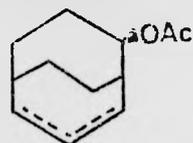
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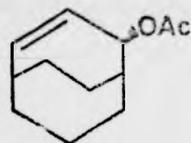
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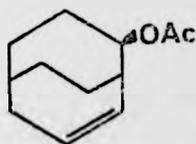
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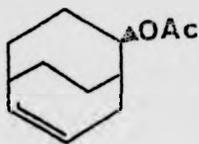
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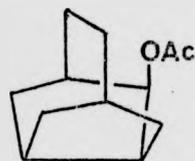
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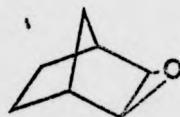
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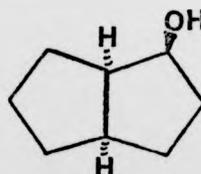
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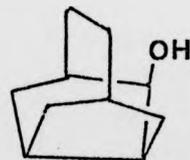
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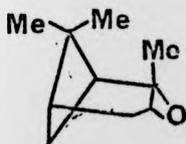
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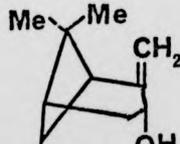
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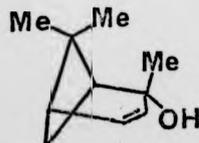
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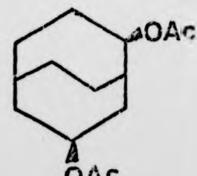
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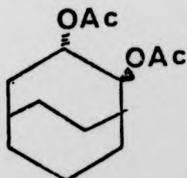
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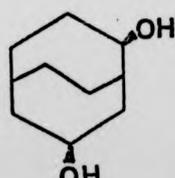
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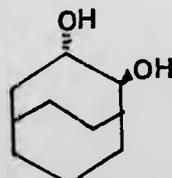
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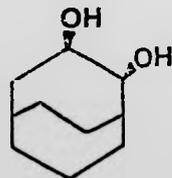
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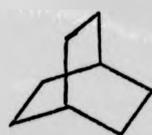
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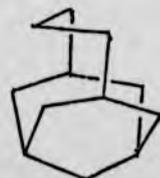
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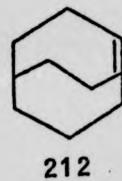
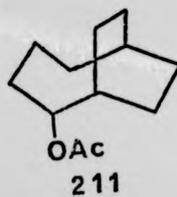
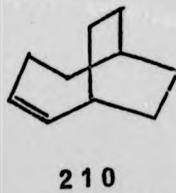
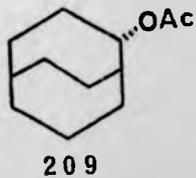
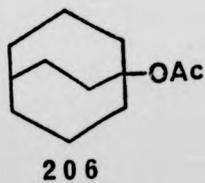
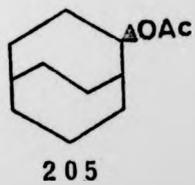
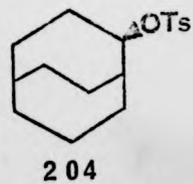
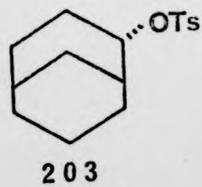
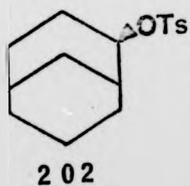
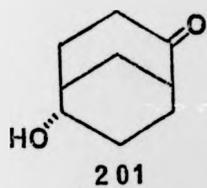
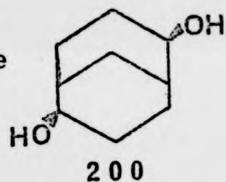
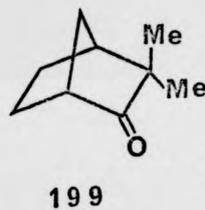
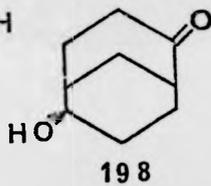
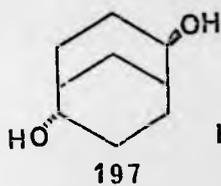
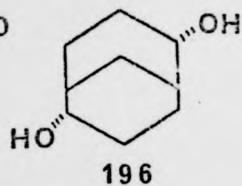
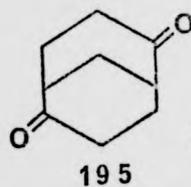
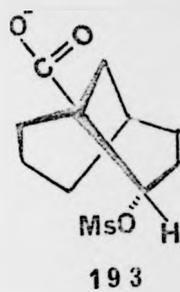
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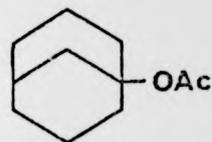


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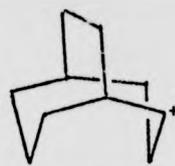


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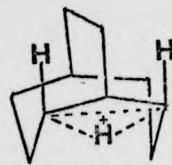




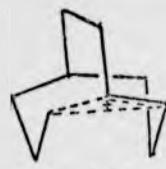
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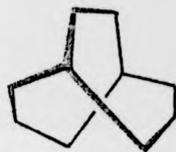
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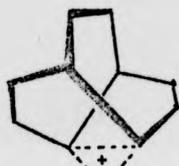
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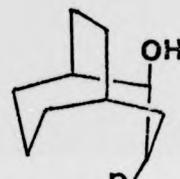
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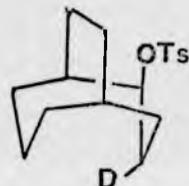
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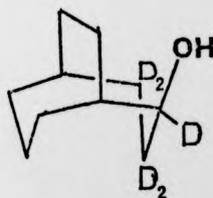
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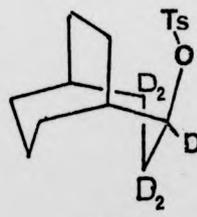
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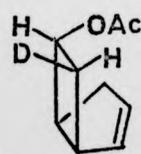
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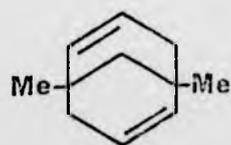
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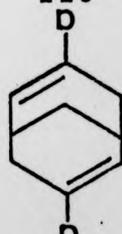
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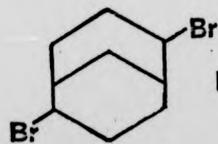
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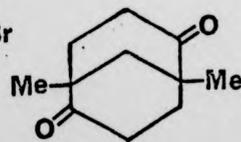
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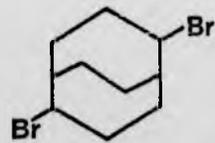
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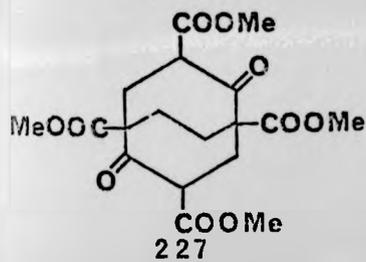
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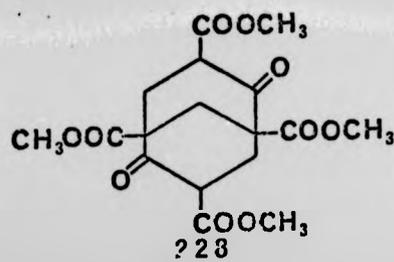
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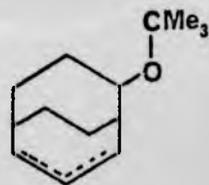
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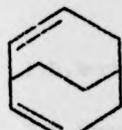
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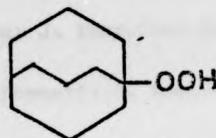
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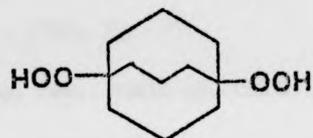
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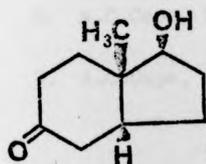
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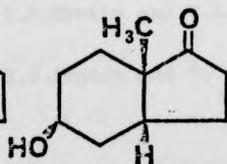
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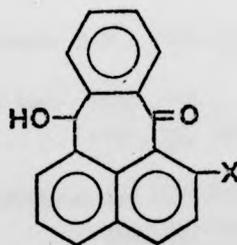
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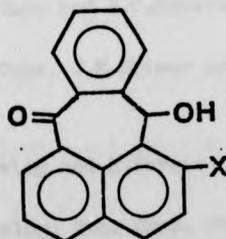
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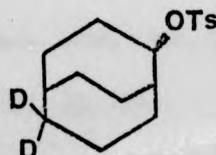
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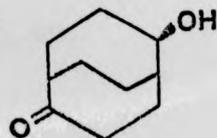
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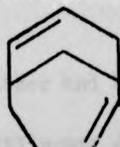
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